Searching for Modifiers of Abelson Tyrosine Kinase Pathway Genes Using Natural Variation in the Drosophila Genetic Reference Panel

Undergraduate Research Thesis

Presented in partial fulfillment of the requirements for graduation with research distinction in

Molecular Genetics in the undergraduate colleges of

The Ohio State University

by

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April 2021

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Abstract

The Abl pathway is involved in many functions within a cell, including axon pathfinding and maintaining the neuronal cytoskeleton. These functions imply a requirement of functional Abl protein within a cell, however, flies that are homozygous mutant for Abl survive to adulthood, although at reduced frequencies. Previous studies have uncovered multiple dosage-dependent modifiers of the Abl^- phenotype, which can either enhance lethality, shifting it toward an earlier developmental stage, or suppress the phenotype, reducing lethality. These studies have yet to examine the effect polymorphic variation within natural population lines has on the dosage-dependent modification of Abl^- phenotype. This study utilizes the inherent genetic variation of the Drosophila Genetic Reference Panel (DGRP) to carry out this analysis. With roughly 200 isogenic lines, the DGRP provides ample natural variation to carry out this investigation. We utilized six sensitized genotypes, five using a balancer chromosome containing the dominant marker, Tubby (Tb), and one using a chromosome containing the dominant marker Drop (Dr). Each genotype allowed us to observe the effect of natural polymorphic variation on the Abl^- phenotype in different ways. We found that the interaction of the DGRP's inherent natural variation and the sensitized backgrounds did affect relative fitness. We also examined the correlation of mean fitness ratios between each genotype and found a range of correlations between multiple genotypes. Calculations of variance both between and within DGRP lines found that total phenotypic variation that was due to genetic differences was surprisingly low. The relative viability of each line in each sensitized background was used in a genome-wide association (GWA) analysis. The GWA analysis produced a list of nearly 200 single nucleotide polymorphisms (SNPs) within the lines that may affect viability of the Abl^- phenotype. These

SNPs occurred in over 100 genes. Additionally, five of those genes were shared between several genotypes.

Introduction

The generation of a nervous system is an incredibly complex, highly regulated process requiring the interactions of hundreds of proteins. While comparatively simpler than vertebrates, Drosophila embryos require the same underlying neural processes to survive (Howard, et al., 2019).To successfully develop, an embryo must coordinate the specification of multiple types of neurons while also controlling how each neuron connects to each other and other cells (Howard, et al., 2019). Guidance of axon growth is controlled through responses to attractive and repressive guidance cues, which guide axons via neuronal receptors to their target regions. Most of these axons are commissural, meaning they cross the midline once to innervate targets on the other side of the embryo and do not cross the midline again (Howard, et al., 2019). There are a host of signaling pathways that regulate guidance to and repulsion from the midline, as axons that aberrantly cross or fail to cross the midline will lead to neural defects.

A signaling protein of particular interest to this study is the Abelson (Abl) tyrosine kinase. The cytoplasmic protein is involved in regulating many crucial cell functions, including axon outgrowth and dynamics of the axon cytoskeleton (Liebl, et al., 2003). Abl interacts with multiple other genes to facilitate axon pathfinding, such as Failed Axon Connections (Fax), Trio, Amalgam (Ama), and Neurotactin (Nrt) (Liebl, et al., 2000) (Liebl, et al., 2003) (Hill, et al., 1995) (Gertler, et al., 1993). Abl is expressed in most tissues during embryogenesis, and in later stages of development, it is localized to the axons of the CNS (Bennett , et al., 1992). Its abundance in developing tissues and extensive interactions implies a necessity of functional copies; however, flies that are homozygous mutant for Abl survive to adulthood at reduced

frequencies, suggesting redundancies in these pathways (Hill, et al., 1995). Through genetic enhancer/suppressor screens, dosage-sensitive modifiers of the Abl^- phenotype have been discovered that increase lethality, shifting it toward an earlier developmental stage (Gertler, et al., 1993). For example, flies that are homozygous mutant for Abl and heterozygous mutant for Nrt die before the pupal stage and exhibit defects in axon pathways within the CNS, although peripheral nervous tissue appears normal (Liebl, et al., 2000). Similarly, heterozygous null mutations of Trio dominantly enhance the Abl^- phenotype (Liebl, et al., 2000). Dominant suppression of the Abl^- phenotype can also occur. Genetic screens have shown that Enabled is a dominant dosage-dependent suppressor of the Abl^- phenotype (Gertler, et al., 1995).

Dosage-dependent modification of the Abl^- phenotype has been a frequent target of genetic screens. This study aims to identify how polymorphic variation that exists within Drosophila natural populations can modify the Abl^- phenotype. While past screens have focused on how single genes can act as modifiers, this study will be examining combinations of polymorphisms that exist in isogenic lines derived from a natural population. A previous study in this lab examined how polymorphic variation within the Drosophila Genetic Reference Panel (DGRP) can affect development of the embryonic CNS axon scaffolding (Gosztyla, 2018). We aim to build on this investigation by utilizing a similar analysis of the effect of the DGRP's inherent variation as dosage-dependent modifiers of the Abl phenotype.

Access to genetically diverse Drosophila lines was made easy through the establishment of the Drosophila Genetic Reference Panel (DGRP). In 2012, researchers created the DGRP using a natural population of flies from Raleigh, North Carolina. By selectively inbreeding the flies, the group was able to create over 200 different isogenic lines (Mackay, et al., 2012). Although each line is isogenic, the DGRP as a whole contains significant genetic variation, with

over 4.6 million single nucleotide polymorphisms (SNPs), 100,000 polymorphic microsatellite sites, and over 30,000 transposable element insertion sites (Mackay, et al., 2012). Additionally, the genome of each line has been fully sequenced, allowing for the correlation of phenotypes with specific genetic variants. Previous GWA studies have demonstrated that the DGRP has substantial natural genetic variation that impacts diverse phenotypes (Mackay, et al., 2018). In this study, a GWA analysis will allow for the identification of polymorphisms that affect viability in different sensitized Abl mutant pathway backgrounds.

The DGRP is a useful tool to analyze gene function. Previous studies have shown that mutations can produce a variety of phenotypes due to the underlying genetic variation of the background in which they are expressed (Mackay, 2014). This approach can also identify genes that are typically missed due to functional redundancy or epistatic interactions. Since its creation, the DGRP has been used to exploit natural variation to assist in the identification of genetic modifiers of specific genes. Recently, the variability of the retinal phenotype Rhl^{G69D} was studied using these mechanisms, and over 100 candidate modifier genes were identified (Chow, et al., 2016). Our study will also utilize the advantages of the DGRP to analyze how genetic variation can affect the ability of enhancers to modulate the Abl^{-} viability phenotype. This analysis may allow for the identification of unknown genes that are components of the Abl pathway.

Methods

This study examined the effect of natural polymorphic variation within the DGRP on relative fitness in different Abl mutant backgrounds. This was accomplished by mating five to six virgin females from a DGRP line with three to four males which contained a sensitized mutant chromosome along with a balancer chromosome encoding a dominant marker. Five sensitized genotypes were used: Abl^{1} Nrt^{M54}/TM6b,Tb (referred to as Abl Nrt throughout the

document), Abl^{1}/TM6B,Tb (Abl^{1}), Abl^{4}/TM6B,Tb (Abl^{4}), P[Abl^{+}]; Abl^{1}, Nrt^{M54}/TM6b,Tb (referred to as Rescue throughout the document), and Comm,$Comm2^{Delta14}$/TM6B,Tb (referred to as Delta 14 throughout the document). The Delta 14 genotype harbors a deletion of the adjacent Comm and Comm2 genes (Seeger Lab unpublished). The Rescue genotype includes an Abl^{+} transgene, inserted on the second chromosome, that rescues phenotypes associated with the Abl^{1} allele on the third chromosome. Additionally, a Dr genotype was created by mating five to six DGRP females to a single male containing +/CyO; Abl^{1} Nrt^{M54}/Dr. The Tb dominant marker created shortened pupae, while the Dr marker created adult flies with small eyes. Both markers allowed for easy scoring of the progeny.

The Abl^{1} and Abl^{4} genotypes were created to show the effect that natural polymorphic variation has on different Abl alleles. The Abl Nrt genotype was used to show if any of those effects could be contributed to Nrt, as the only difference between Abl^{1} and Abl Nrt was the presence of the Nrt^{M54} allele. The Rescue genotype included a wild-type copy of Abl with the Abl Nrt chromosome, to test if normal viability could be "rescued" with the addition of functional Abl. The Delta14 genotype served as a control, as deletions in the two Comm genes aimed to test how mutations in other neuronal genes would affect viability. The Dr genotype served as an additional control by testing if the viability of the other genotypes could be attributed to interactions with the Tb chromosome.

Flies were brooded at four and eight days after mating, and vials were cleared after 12 days. At 15-16 days after egg laying, the progeny were scored. Scoring involved counting the number of Tb^{-} and Tb^{+} pupae on the walls of the vials. For the Abl Nrt genotype, at least five scored crosses per line with a minimum of 50 pupae total was set as a threshold for our experimental pipeline. For the other four Tb genotypes, at least three crosses of each line were

scored with a minimum of 50 pupae scored per cross. Adult progeny from crosses using the Dr marker were sorted and counted in four categories: Dr^+ and Dr^- females, and Dr^+ and Dr^- males, and only flies that were Cy^+ were scored. Adult flies were scored for the final time at 20 days after egg laying. The more restrictive end point of scoring for Dr flies meant that a different endpoint is being accessed. Tb flies only had to survive to the pupal stage, while Dr flies had to survive to adulthood.

After total calculations were complete for each DGRP line with each of the genotypes, the data was entered into Excel for analysis. The total count of pupae/flies was entered, along with the date of the initial cross. The ratio of Tb^+/Tb^- or Dr^+/Dr^- flies was calculated for each dated entry, and the mean Tb^+/Tb^- or Dr^+/Dr^- ratio within each DGRP line was also calculated. The standard deviation of the individual ratios, the mean count of flies in each category, and the standard deviation of the mean count of flies were also calculated for each line. The correlation of these relative viability ratios to the total number scored for each cross was also included. A sample data entry table can be seen in Table 1.

This data was condensed into a table that contained each DGRP line, its mean ratio, standard deviation of ratios, correlation, mean count, and standard deviation of mean counts, and was repeated for each genotype. Calculations were only done on DGRP lines that had at least three dated entries (five for Abl Nrt) with a minimum total of 50 pupae/adults counted. Lines with less than three entries were still added into Excel but were not included in data analysis. The mean Tb^+/Tb^- or Dr^+/Dr^- ratio was our main focus of data analysis. Each line's mean ratio for a genotype was sorted into increasing order and was graphed for each genotype. Additionally, graphs showing the correlation of a line's mean ratio between sensitized backgrounds were also produced. The variation of ratios both within lines and mean ratios between lines was also

calculated. Average variation within lines was calculated as the squared mean of individual line standard deviations. Variation between lines was found by calculating the standard deviation of all the mean ratios for a sensitized background and squaring the value. The number of lines with ratios above and below 1.0 was calculated and placed into a table, and a table including the differences between the largest and smallest ratios for each genotype was produced. Finally, a table containing a ranked order list of the mean ratios for each genotype was created.

DGRP lines paired with their mean ratios were submitted to the DGRP2 pipeline for GWA analysis (http://dgrp2.gnets.ncsu.edu). This pipeline shows SNP results that have a p-value of at least 10^{-5}. Minor alleles with a frequency below 5% were not included in the results. The SNP data was condensed into a table which contains the SNP name, its site annotation (intron, exon, 5'UTR, among others), the gene name where the SNP occurs (if applicable), the p-value, and the sensitized backgrounds the data originated from.

Results/Discussion

The distribution of mean Tb^+/Tb^- ratios with the Abl Nrt sensitized background appears linear for most of the data set, but as the mean ratios near the upper quartile, the data begins to increase exponentially (Figure 1). The majority of lines within this genotype had mean Tb^+/Tb^- ratios below 1.0 (Table 3). Lines with a ratio above 1.0 contained fewer flies with the Tb balancer chromosome than without, and therefore contained more flies with the mutated Abl Nrt genotype than without. In these lines, the chromosome with the Abl Nrt mutation had a higher relative fitness. As the majority (63%) of Abl Nrt lines had a ratio below 1.0, mutations in both Abl and Nrt appear to be deleterious and the relative fitness of flies carrying both mutations was decreased (Table 3). The variation of mean ratios within lines of the Abl Nrt genotype was larger than the variation between lines in the genotype (Table 5). This pattern was consistent

throughout all genotypes. Variation between lines describes the genetic component of phenotypic variation, and variation within lines describes environmental effects. As variation within lines was consistently larger than between lines, it indicates that the observed phenotypic variation was due more to environmental effects than genetic differences. To further investigate this, total phenotypic variation was also found for each genotype. By dividing the between line variation by total phenotypic variation, we were able to estimate how much of the total phenotypic variation can be attributed to genetic differences. These results were also consistently low (Table 5). We anticipated the percentage of phenotypic variation due to genetic differences to be higher than what we observed, implying that we underestimated the role of nongenetic differences in the total phenotypic variation. We also expect that the large variation found within lines limited our ability to identify variation between lines. The range of ratios across the DGRP was also relatively small, further hindering our ability to identify genetic variation.

Abl^1 and Abl^4 both had a majority of lines with mean ratios above 1.0, indicating that mutations in only the Abl allele were not a deleterious as mutations in both Abl and Nrt. The distribution of mean Tb^+/Tb^- or Dr^+/Dr^- ratios was unique to each genotype, as was the number of lines with ratios above or below 1.0 (Figures 1-2, Table 3). However, each genotype followed a basic pattern of gradually increasing ratios up until the last few lines, where ratios began to increase much more rapidly (Figures 1-2). Between all the genotypes, no ratio was lower than 0.475 and no ratio was larger than 2.972. The average difference between the largest and smallest mean ratios throughout all genotypes was 1.56 (Table 4). Overall, 57% of lines throughout all genotypes had mean ratios above 1.0. The distribution of mean ratios was the most extreme within the Delta 14 genotype. Within that genotype, only four lines had ratios below 1.0 (Table 3). This implies that the deletion of one copy of both Comm and Comm2 was

not as deleterious of a mutation as any of the Abl mutations. Among the Abl mutant genotypes, Abl^4 had the highest relative fitness, with 87% of DGRP lines having a mean Tb^+/Tb ratio above 1.0 (Table 3).

Ranked-order lists of mean Tb^+/Tb ratios in each genotype were produced to further examine the mutant genotype's role in affecting viability. The highest-ranking mean Tb^+/Tb ratio within a genotype, which was the line that showed the highest relative fitness with the mutant genotype was ranked 1 (Table 2). The genotypes we introduced into the DGRP backgrounds do seem to influence the viability ratios. The effect on viability did not need to be in one direction. The interaction of natural polymorphisms within the DGRP and the mutant genotypes could have increased or decreased relative fitness. We were interested in examining the extent of that interaction, not its direction. Many lines had considerable differences in their mean Tb^+/Tb^- ratios between genotypes (Table 2). However, some lines did show consistency in their rankings. Line 374 was in the bottom 5% of lines for four of the five genotypes and was in the bottom quartile for the fifth genotype (Table 2). Conversely, line 714 was consistently ranked in the top 10 for every genotype (Table 2). Lines whose rankings did not change much indicate that their background variation's interaction with the genotype of the sensitized background was minimal. It also implies that the interaction of the DGRP polymorphisms with the Tb chromosome was the major driver of relative fitness, instead of interactions between the DGRP and sensitized backgrounds. We hypothesized that the genotype with the greatest impact on viability would be Abl Nrt, followed by Abl^1, and Abl^4. This pattern was seen in some lines and was absent in others. Line 427 follows this pattern, as its interaction with mutant genotypes was most extreme with Abl Nrt, followed by Abl^1 and Abl^4 (Table 2). The shift in ranking seen with Rescue indicates that adding Abl functionality restored some relative fitness of that genotype. Line 350

is an example of a line that did not follow this pattern. It was remarkably consistent in its rankings, apart from Delta 14 (Table 2). In this line, the interaction of Comm or Comm2 with the DGRP background was more extreme than in other lines. Additionally, line 100 ranked first (the highest) for mean ratios in the Abl^1 genotype, but was ranked near the bottom for the Abl Nrt, Abl^4, and Rescue genotypes. This implies that mutations in Nrt in this line affected viability to a much lesser extent than mutations in either of the other Abl genotypes. The effect of the interaction of each genotype and DGRP backgrounds on viability and therefore the ranking was unique to each DGRP line. The lack of consistency in some genotypes makes more sense when considering the limited role genetic differences played in total phenotypic variation (Table 5). Had variation due to genetic differences had more of an effect on total phenotypic variation, we would expect to see much more consistent rankings within a single line. An initial comparison with data gathered in this lab's previous work does not reveal consistent patterns between the DGRP line's relative fitness and axon guidance defects (Gosztyla, 2018).

We looked for correlations of mean ratios between different sensitized backgrounds. We would expect that Delta 14 would not correlate with the various Abl mutant backgrounds. This was observed with correlations ranging from 0.170 to 0.298 (Table 6 and Figures 6, 10, 11, and 13). Mean ratios for Abl Nrt were correlated at a similar, mild, degree to Abl^1 and Abl^4, and were correlated much more to Rescue than to Delta14 (Table 6). We expected to see a correlation between the Abl mutant genotypes if changes to viability were due to Abl. As the correlation between Abl mutant genotypes was milder than expected, this lends further weight to the role of nongenetic differences in affecting viability. The effect of polymorphic variation within the DGRP lines on viability was most similar between Abl Nrt and Rescue, but that similarity was not extreme. We expected to see a correlation between Abl Nrt and Rescue, but we did not

expect it to be the strongest correlation we found. There was some degree of correlation in each combination of lines, except for the Abl Nrt and Dr genotypes (Table 6). This was surprising, as we initially hypothesized that these two genotypes would show the highest degree of correlation. This suggests that the Dr and Tb chromosomes may be affecting viability more than we initially thought, and they are affecting viability in different ways. Graphs of the mean ratios between each combination of genotypes were created to further examine correlation (Figures 4-14). These again showed no extreme correlation in any pair of genotypes, however, Abl Nrt vs Abl^1 and Abl Nrt vs Abl^4 showed a slight correlation of ratios (Figures 4-5).

The Dr genotype's mean Dr^+/Dr^- ratios were also graphed in increasing order (Figure 3). The shape of its distribution was similar to the other genotypes, but the change in mean ratios was less drastic at either end. The Dr genotype had by far the largest percentage of lines with a mean ratio below 1.0, indicating that the relative fitness of this genotype was much less than that of all other genotypes (Table 3). This may be partially explained by the more restrictive endpoint of scoring that we used for the Dr flies. Dr flies were scored as adults, while Tb flies were scored as pupae. By increasing the amount of time the flies needed to survive before being scored, we allowed more time for fitness to decrease due to detrimental interactions between the DGRP polymorphisms and sensitized backgrounds.

Submitting the DGRP lines paired to their mean ratios for GWA analysis produced a list of 187 SNPs, which occurred in 103 genes (Table 7). Each genotype was submitted individually, but the data was condensed together into a single table (Table 7). 47 of the SNPs did not occur within genes, and instead were intergenic modifiers (Table 7). This distribution is consistent with the distribution of polymorphisms in the DGRP. These SNPs included many transcription factor binding sites. Most SNPs that occurred within a gene occurred within introns (Table 7). Only one

SNP from all genotypes occurred in an exon (Table 7). Other regions where SNPs occurred include 5' and 3' UTRs, and synonymous or non-synonymous coding regions. We did not see extensive overlap in the genes that the SNPs corresponded to. Of the 103 genes where SNPs occurred, only five were shared between different genotypes (Table 8). The less than expected role of genetic differences in phenotypic variation may be attributing to the difficulty in identifying shared genes with SNPs between genotypes. Had genetic differences accounted for a larger percentage of total phenotypic variation, we hypothesize that we would have found many more genes in common. However, all five genotypes did share genes where SNPs occurred with at least one other genotype. These genes were CG1887 (also known as dsb), CG32365, cv-c, mbl, and Pde1c (Table 8). These genes did not have specific functions within the Abl pathway but did control other cell functions like morphogenesis, synaptic homeostasis, cell organization, and neural differentiation. Interestingly, cv-c encodes a RhoGTPase activating protein (GAP), which interact extensively with Rho guanine nucleotide exchange factors (GEFs) (Denholm, et al., 2005). As Trio encodes a GEF, these proteins may interact within the cell. However, because cv-c was only identified in GWA results from a single genotype, we are hesitant to remark on the extent or significance of this interaction. Within a single genotype, it was common for a gene to appear more than once. For example, four SNPs from the Rescue data set occurred in the Ance-3 gene, and four SNPs from the Abl^4 genotype occurred in the osp gene (Table 7).

Summary

Mean Tb^+/Tb^- ratios were used to examine the effect of natural variation within the DGRP on relative fitness within sensitized backgrounds. Lines with a mean ratio above 1.0 contained more flies with the sensitized genotypes than with the Tb^- balancer chromosome or Dr^- chromosome. The interaction of the DGRP's genetic variation and our sensitized genotypes did

seem to have an effect on viability. The extent and direction of that effect were unique to each genotype. The relative fitness of each genotype was also unique, as some genotypes like Abl Nrt had lower relative fitness, and others such as Abl^{1} and Abl^{4} had a higher relative fitness. The Delta 14 genotype showed the most positive effects on relative fitness, as only four lines had mean ratios below 1.0. We did not see an extensive correlation between the mean ratios of the sensitized backgrounds, which was not what we originally hypothesized. This may reflect a combination of interactions of the DGRP genotype with both the sensitized background and the Tb^{-} balancer or Dr^{-} chromosomes. We also saw that phenotypic variation due to genetic differences was much less than we originally anticipated. The large amount of variation within lines limited our ability to reliably identify variation between lines. This was compounded by the relatively limited range of mean ratios between all DGRP lines. In future extensions of this investigation, we aim to include a more neutral control group (an unsensitized background) that may help account for this effect. These control groups would allow us to establish a baseline value we can use to compare with different sensitized backgrounds. Relative viability is a difficult endpoint to assess with the DGRP. Teasing out how each DGRP line interacts with the Tb^{-} balancer (or Dr^{-} chromosome) versus the sensitized background chromosome (e.g., Abl Nrt) is complex, especially given the large contribution of environmental variation to the total phenotypic variance. We have concluded that additional and better controls would be helpful in this process.

Table 1. The Excel table built for DGRP line 21 with the Abl Nrt sensitized background. This is a representative example of the tables built for each DGRP line with each sensitized background. The total column is the total count of pupae/flies for that individual dated entry. The total row is the total count of pupae/flies for all dated entries. Mean of ratios was calculated by taking the average Tb^+/Tb^- ratio of each dated entry. Correlation is the correlation between the Total column and the Tb^+/Tb^- column. Mean count is the average of the values found in the Total column and represents the average pupae/flies counted between all dated entries for that DGRP line. Standard deviation of ratios and standard deviation of mean count represent the standard deviation of the Tb^+/Tb^- column and Total column, respectively. Mean of ratios, standard deviation of ratios, correlation, mean count, and standard deviation of mean count all did not include the values in the Total row when calculations were made.

DGRP #	Date	# Tb-	# Tb +	Total	Tb+/Tb-	Mean of ratios	St. Dev of ratios	Correlation	St. Dev of mean count	Mean Count
21	11/22	65	40	105	0.615	0.722	0.352	0.790	40.96	117.8
21	11/22	64	73	137	1.141					
21	11/22	82	32	114	0.390					
21	2/16	84	88	172	1.048					
21	3/21	43	18	61	0.419					
Total		**338**	**251**	589	0.743					

Table 2: A ranking of each DGRP line's mean Tb+/Tb- ratio compared to all other lines, for each genotype. The highest mean Tb+/Tb- ratio is ranked 1. Blank spaces indicate that the DGRP line either was not scored for that genotype or did not reach the scoring threshold. A three-color gradient scale was used to represent values. The darkest green was used for the maximum values within the ranking, which represent lines with the lowest mean ratios. Red was used for lines with the highest mean ratios, and yellow was used for lines in the 50th percentile. After assigning colors to the minimum, maximum, and 50th percentiles, Excel applied a gradient throughout the table.

Line	Abl Nrt	Abl 1	Abl 4	Rescue	Delta 14
21	168	154	50	105	114
26	47	36	63	56	67
31	23	68	34	27	74
32	22	123	118	94	125
38	72	62	88	74	50
40	105	115	173	112	24
41	176	34	180	157	130
42	116	6	126	48	42
45	164			161	5
57	62	125	38	84	146
59	87	75	161	137	12
69	154		70		
73	12	49	81	117	152
75	56	63	141	168	138
83	82	72	76	135	71
85	113	131	31	118	91
88	13	15	9	24	66
91	64	138	171	70	126
93	21	33	97	54	78
100	132	1	178	116	22
101	84	38	56	102	11
105	122	94	74	133	175
109	107	163	72	152	170
129	160	18	25		29
136	126	150		88	107
138	181	130	142	129	100
142	81	92	168	125	158
149	52	44	8	16	95
153	129	126	18	53	112
161	115	148	157	127	167
177	163	16	15	136	119
181	155	86	33	13	38
189	80	173	22	167	
195	70	41	43	12	173
208	28	81	45	17	21
217	10	3	36	6	
227				169	117
228	40	168	147	146	172
229	60	113	129	58	49
235	38	71	32	73	103
237	111	129	39	52	106

Line	Abl Nrt	Abl 1	Abl 4	Rescue	Delta 14
239	101	124	104	144	143
256	16	28	20	18	2
280	166	26	169	79	18
287	11	7	11	2	72
301	145	156	78	21	168
303	182	183	176	134	164
304	144	117	37	171	145
306	27	140	105	114	153
307	165		10	78	
309	123	48	3	92	97
310	110	88	146	131	9
313	63	112	54	121	111
315	131	111	160	34	51
317	147	167	65	29	57
318	95	46	7	139	109
319	24	39	68	7	8
320	26	120	73	104	116
321	5	182	51	43	88
324	73	134	44	41	179
332	187	172	172	154	
335	86	32	4	68	52
336	149	141	117	142	132
338	67	103	112	120	165
340	109	116	89	166	48
348	83	161	95	49	139
350	185	184	182	181	59
352	119	97	166	160	163
354	37	27	86	143	63
355	61	57	13	26	142
356	59	80		124	133
357	29	52	149	3	127
358	171	176	151	163	68
359	14	51	48	28	28
360	103	102	93	111	141
361	136	73	110	174	176
362	174	178	158	184	73
365	17	174	59	86	160
370	169	65	154	156	44
371	98	64	165	39	174
373	146	171	99	153	150
374	184	149	184	188	182

Table 2. (continued)

Line	Abl Nrt	Abl 1	Abl 4	Rescue	Delta 14
375	57	76	62	72	96
377	19	29	120	80	98
379	45	170	127	51	162
380	108	147	135	82	
381	106	106	167	99	36
382	39	105	153	50	137
383	96	89	116	110	181
385	121	155	139	23	14
386	49	109	17	45	87
390	188	144	150	187	151
391	6	2	125	1	157
392	104	145	123	87	134
395	34	42	82	38	53
397	134		144	108	
399	66	121	12	81	27
405	68	50	69	44	148
406	9	45	6	69	70
409	8	37	75	11	136
426	36	70	175	40	102
427	159	146	115	95	75
437	4	9	14	22	46
439	41	8	58	32	20
440	172	17	140	128	89
441	99	139	155	132	16
443	167	110	137	91	85
461	54	82	159	37	128
486	30	93	96	119	23
491		114			166
492	183	11	183	179	79
502	18	56	77	66	26
505	189	77	181	162	81
508	7	79	16	97	31
509	97	23	134	98	6
513	71	54	145	8	58
517	35	53	24	57	113
528	137	160	102	183	80
530	88	13	84	60	123
531	125	43		103	61
535	150	158	94	155	161
551	170	142	164	175	122
555	100	151	5	67	13

Line	Abl Nrt	Abl 1	Abl 4	Rescue	Delta 14
559	69	87	30	77	131
563	143	162	71	113	84
566	128	165	136	177	69
584	48	96	133	59	90
589	78	60	46	71	39
595	173	166	163	150	110
596	3		177	10	
627	2	10	1	5	33
630	120	132	66	182	30
634	180	179	179	147	37
639	53	22		75	15
646	102	98	107	122	94
703	130	5	103	61	25
705	65	55	47	89	32
707	51	90	91	164	108
712	186	104	152	185	155
714	1	4	2	9	4
716	76	157	124	115	120
721	141	78	111	172	115
730	43	21	156	63	118
732	179	153	148	159	1
737	58	20	121	4	35
738	46	128	52	65	56
748	32	107	55	14	156
757	142	181	128	170	180
761	139	127	80	158	47
765	152	122	106	106	60
774	33	58	53	85	77
776	25	137	49	107	19
783	156	91	28	141	45
786	151	133	98	165	41
787	15	108	87	64	83
790	74	100	90	36	177
796	175	177	35	145	104
799	162		130	76	43
801	31	69	67	35	129
802	118	74	143	31	64
804	140	25	79	180	154
805	94	31	21	33	55
808	138	180	132	178	149
810	124	84	26	130	140

Table 2. (continued)

Line	Abl Nrt	Abl 1	Abl 4	Rescue	Delta 14
812	75	59	92	100	10
818	157	175	138	186	169
819	190	136	109	176	40
820	42	119	101	42	121
821	50	169	100	101	101
822	112	118	108	47	159
832	90	83	174	123	171
837	161	95	162	173	34
843	91	12	23	46	86
850	79	47	61	149	7
852	177	135	131	93	147
853	148	35	119	55	124
855	117	152	57	148	93
857	93	30	41	138	82
859	92	85	40	30	135
861	153	101	27	151	17
879	133	66	19	140	144
880	55				
882	135	24	170	90	65
890	127	164	64	96	105
892	44	19	83	15	3
897	85	40	29	25	54
900	114	143	60	109	99
907	89	61	122	20	76
908	178	14	42	83	92
911	158	159	113	62	178
913	20	67	85	19	62
Control	77	99	114	126	

Table 3. The number of DGRP lines with mean Tb^+/Tb^- ratios above and below 1.0 for each genotype. The percentages of total lines in that genotype that fell into either category was also included. The Dr genotype uses mean Dr^+/Dr^- ratios.

Genotype	Abl Nrt	Abl 1	Abl 4	Rescue	Delta 14	Dr
# of lines with ratio below 1.0	120 (63%)	85 (46%)	24 (13%)	102 (54%)	4 (2%)	128 (86%)
# of lines with ratio above 1.0	70 (37%)	99 (54%)	160 (87%)	86 (46%)	178 (98%)	21 (14%)

Table 4. The differences between the largest and smallest mean ratio for each genotype, as well as the average difference throughout all genotypes.

Genotype	Abl Nrt	Abl 1	Abl 4	Rescue	Delta 14	Dr
Difference between largest and smallest mean ratio	1.72	1.42	2.50	1.55	1.70	0.46
Average difference	1.56					

Table 5. Variation (s^2) of mean ratios within lines in a genotype, variation (s^2) between all the lines in a genotype, total phenotypic variation (s^2), and the percentage of phenotypic variation that can be attributed to genetic differences within DGRP lines. Variation within lines was calculated by squaring the mean of individual line standard deviations within a genotype. Variation between lines was calculated by taking the standard deviation of all mean ratios in a genotype and squaring the value. Total phenotypic variation was calculated by taking the standard deviation of all individual ratios in a genotype and squaring the value. Variation due to genetic differences is the variation between lines divided by total phenotypic variation. Values were rounded to four decimal points for the table, but percentages were calculated using the full values.

Genotype	Variation within lines	Variation between lines	Total Phenotypic Variation	Variation Due to Genetic Differences
Abl Nrt	0.0509	0.0028	0.1080	2.56%
Abl 1	0.0257	0.0023	0.0691	3.29%
Abl 4	0.0647	0.0061	0.1398	4.37%
Rescue	0.0350	0.0036	0.0928	3.85%
Delta 14	0.0452	0.0039	0.1108	3.48%
Dr	0.0257	0.0001	0.0329	0.28%

Figure 1. Mean Tb^+/Tb^- ratios of Abl Nrt shown in increasing order. Each blue circle represents a single DGRP line. Error bars represent the standard deviation of that line.

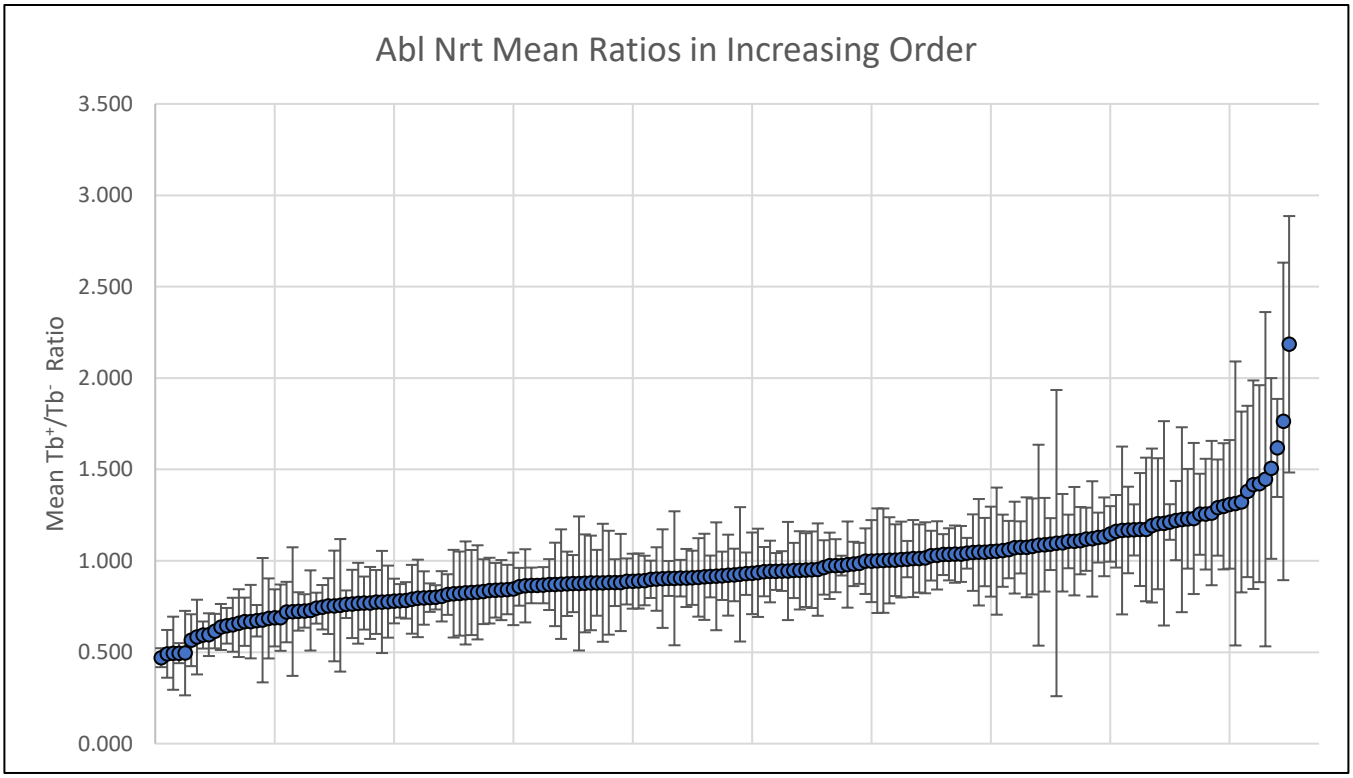

Figure 2. Mean Tb^+/Tb^- ratios of Abl^1, Abl^4, Rescue, and Delta 14 shown in increasing order. Each blue circle represents a single DGRP line. Error bars represent the standard deviation of that line.

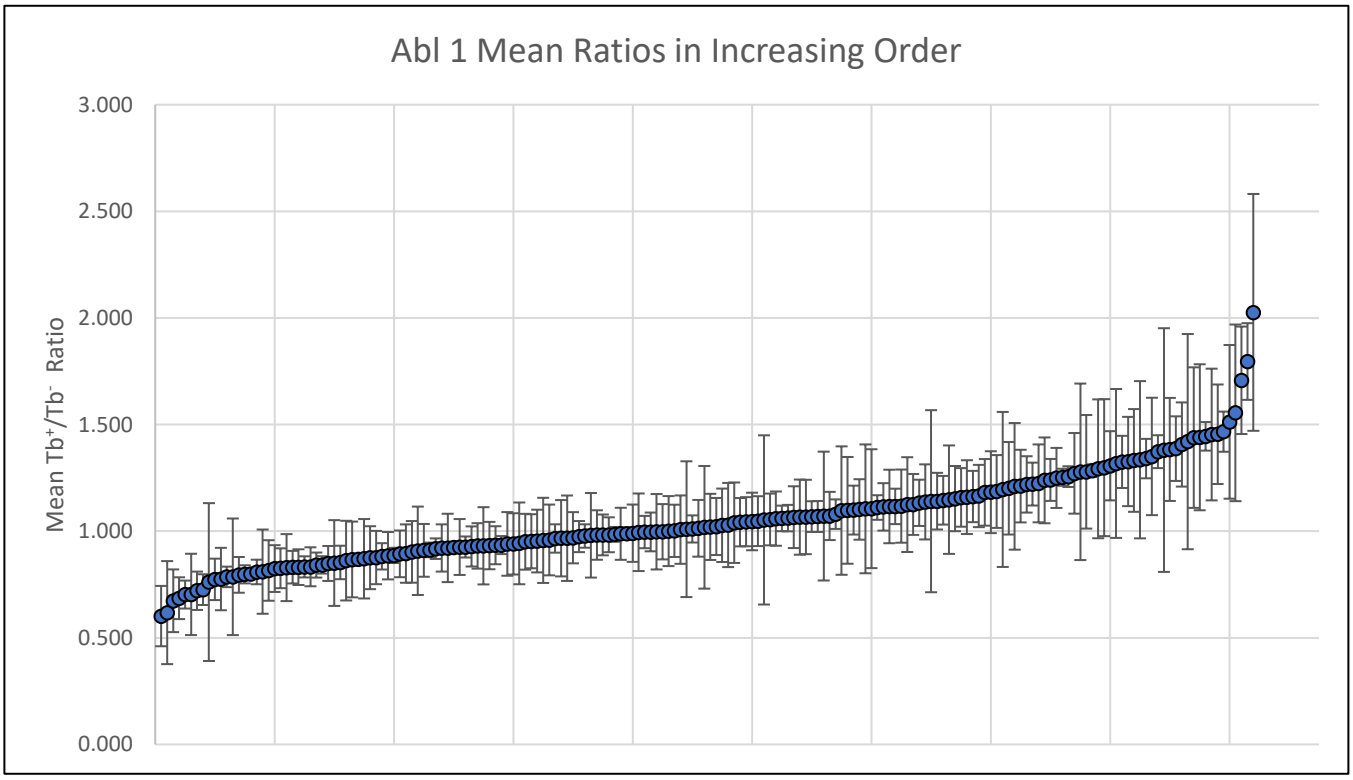

Figure 2. (continued)

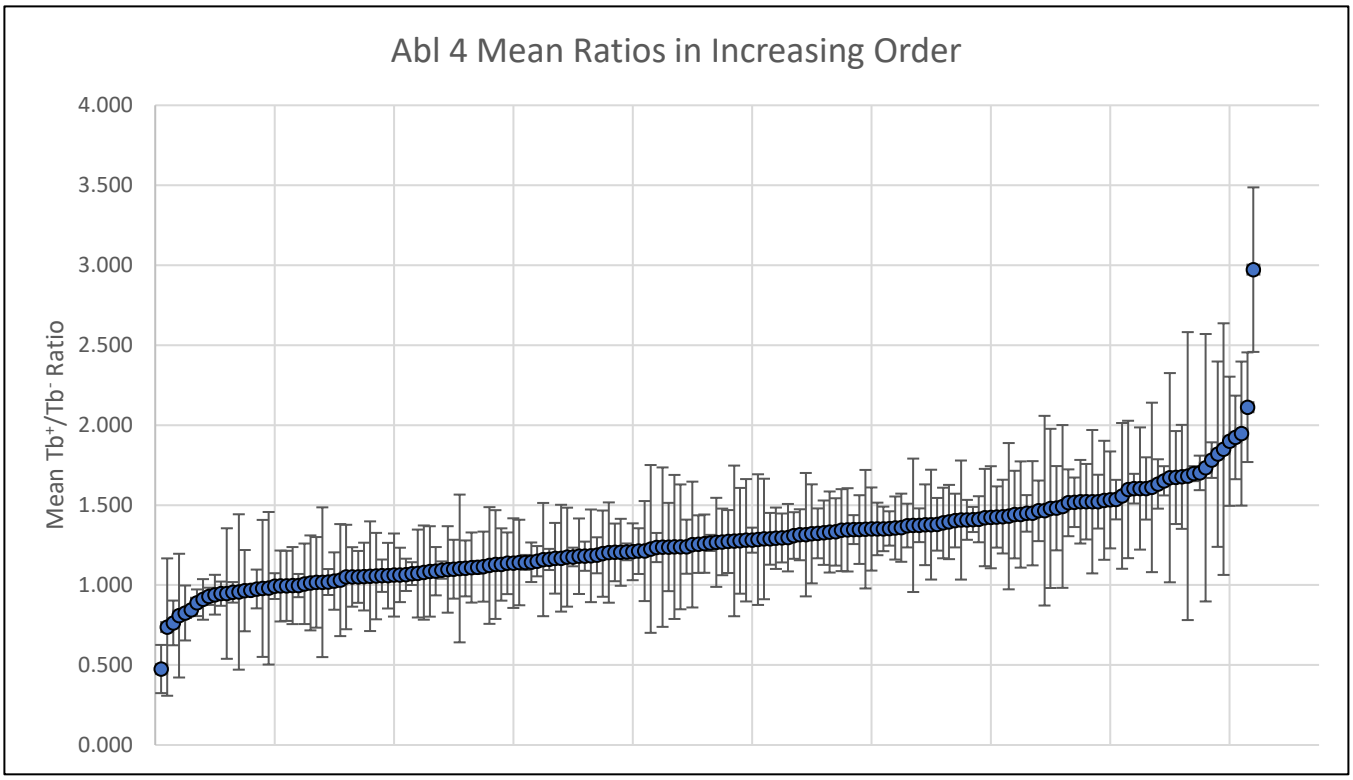

Figure 2. (continued)

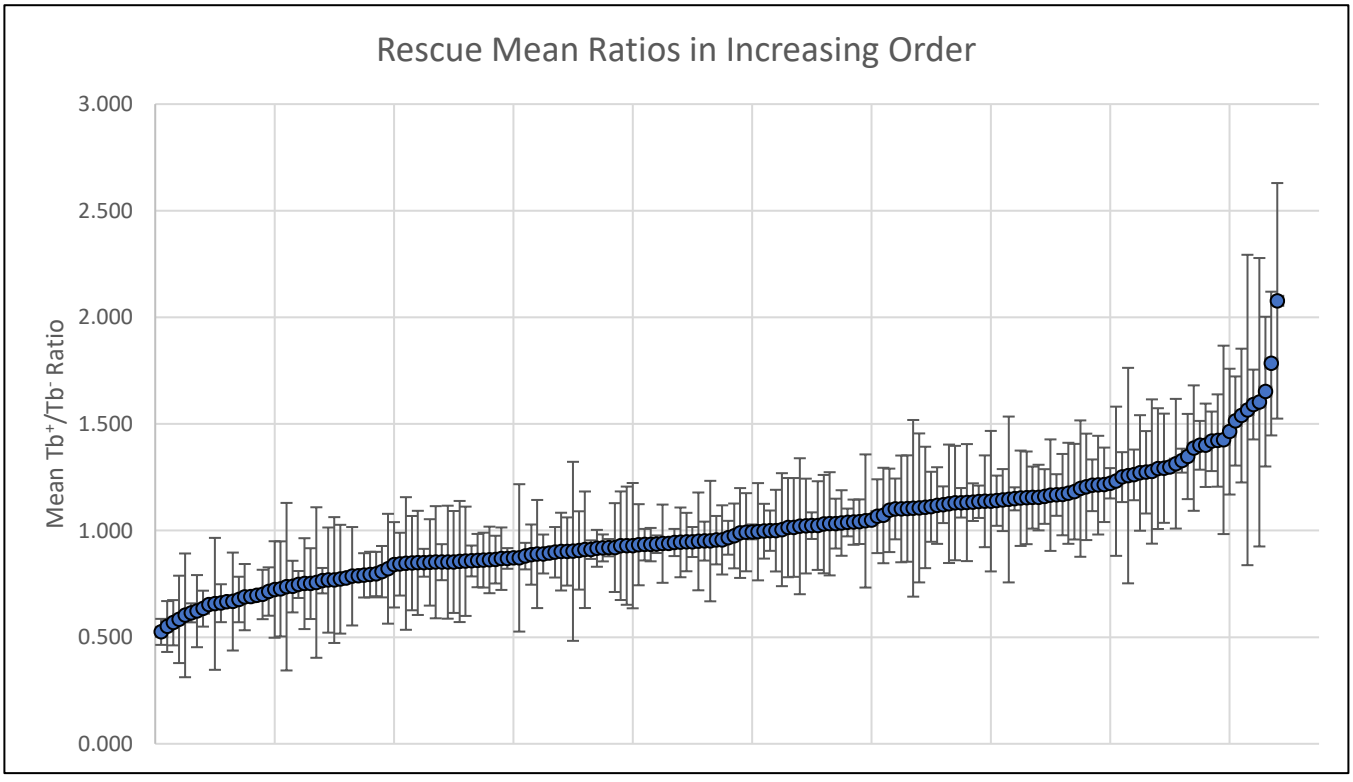

Figure 2. (continued)

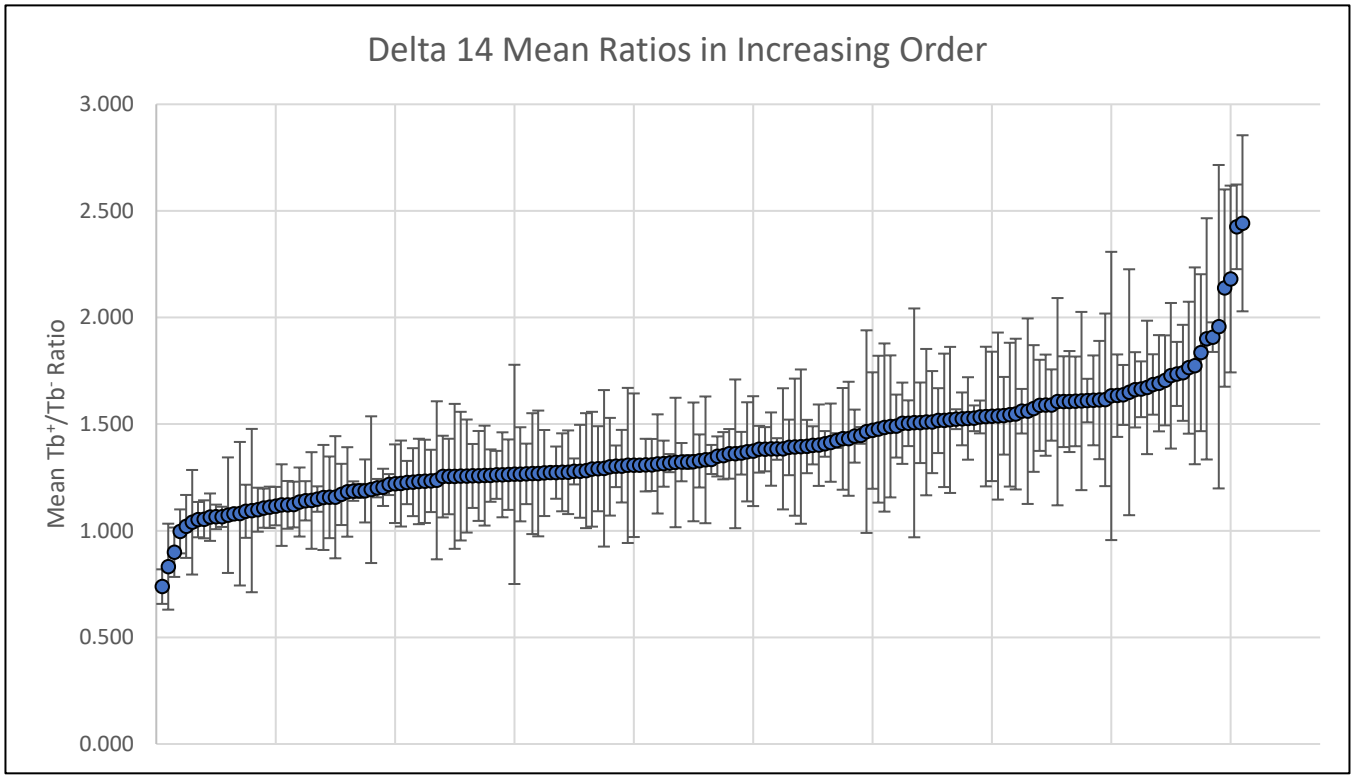

Figure 3. Mean Dr^{+}/Dr^{-} ratios of Abl Nrt/Dr shown in increasing order. Each blue circle represents a single DGRP line. Error bars represent the standard deviation of that line.

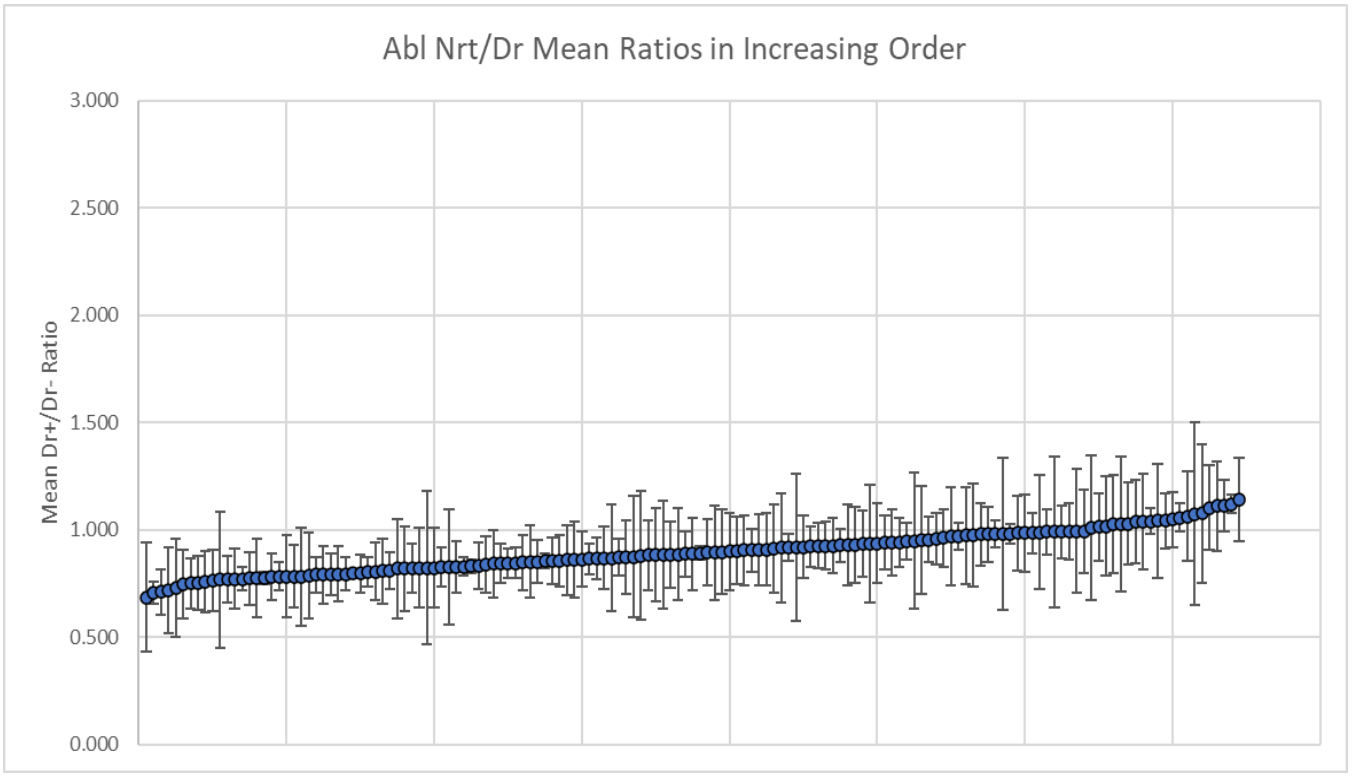

Table 6. The correlation of each line's mean Tb+/Tb- ratio between different genotypes. Abl Nrt Tb vs Abl Nrt Dr is a correlation between Abl Nrt's mean Tb+/Tb- and Dr+/Dr- ratios.

Correlations of mean ratios	
Abl Nrt vs Abl 4	0.471
Abl Nrt vs Abl 1	0.380
Abl Nrt vs Delta 14	0.170
Abl Nrt vs Rescue	0.623
Abl 1 vs Abl 4	0.244
Abl 1 vs Rescue	0.479
Abl 1 vs Delta 14	0.298
Abl 4 vs Delta 14	0.187
Abl 4 vs Rescue	0.350
Rescue vs Delta 14	0.171
Abl Nrt Tb vs Abl Nrt Dr	0.005

Figure 4. A graph of Abl Nrt's mean Tb+/Tb- ratio vs the mean Tb+/Tb- ratio of Abl 4.

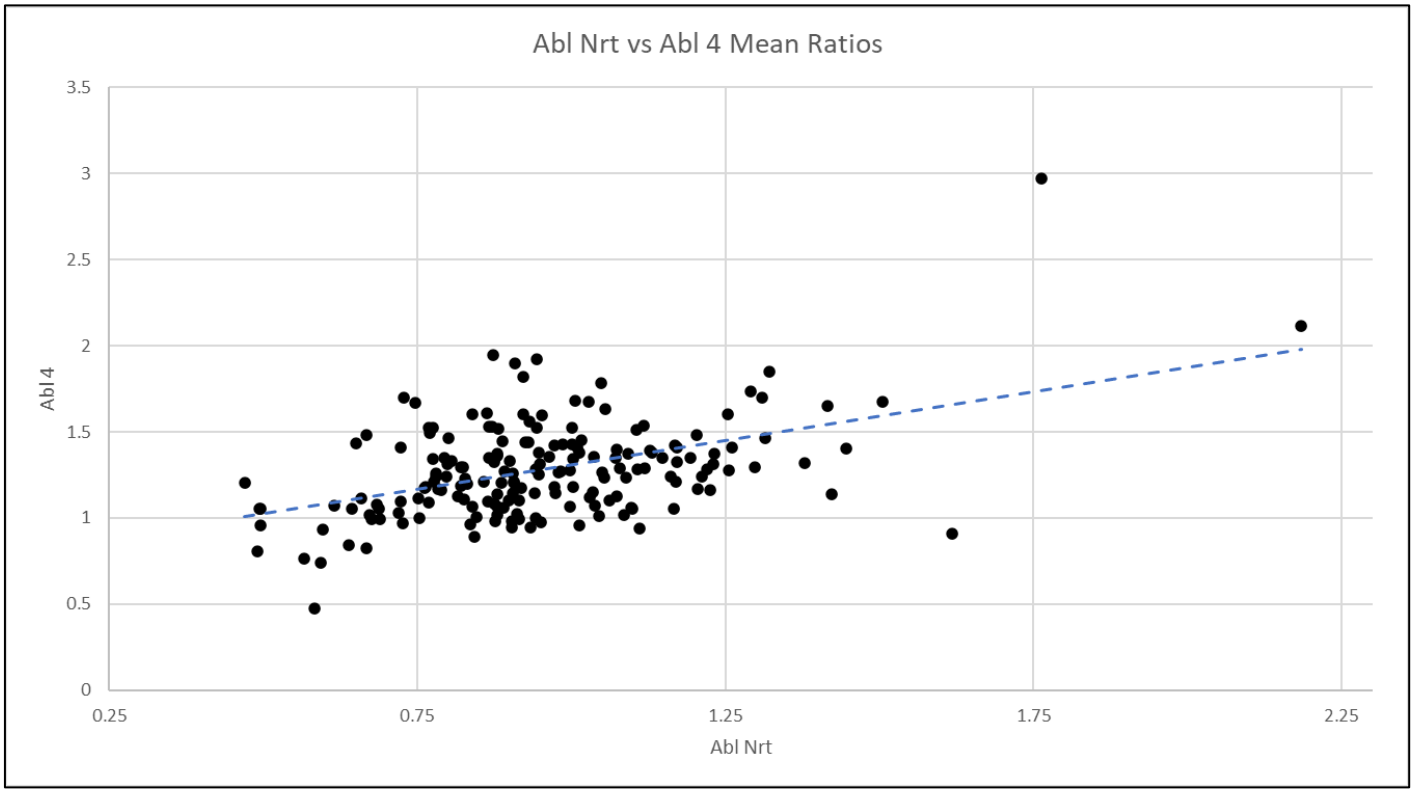

Figure 5. A graph of Abl Nrt's mean Tb+/Tb- ratio vs the mean Tb+/Tb- ratio of Abl 1.

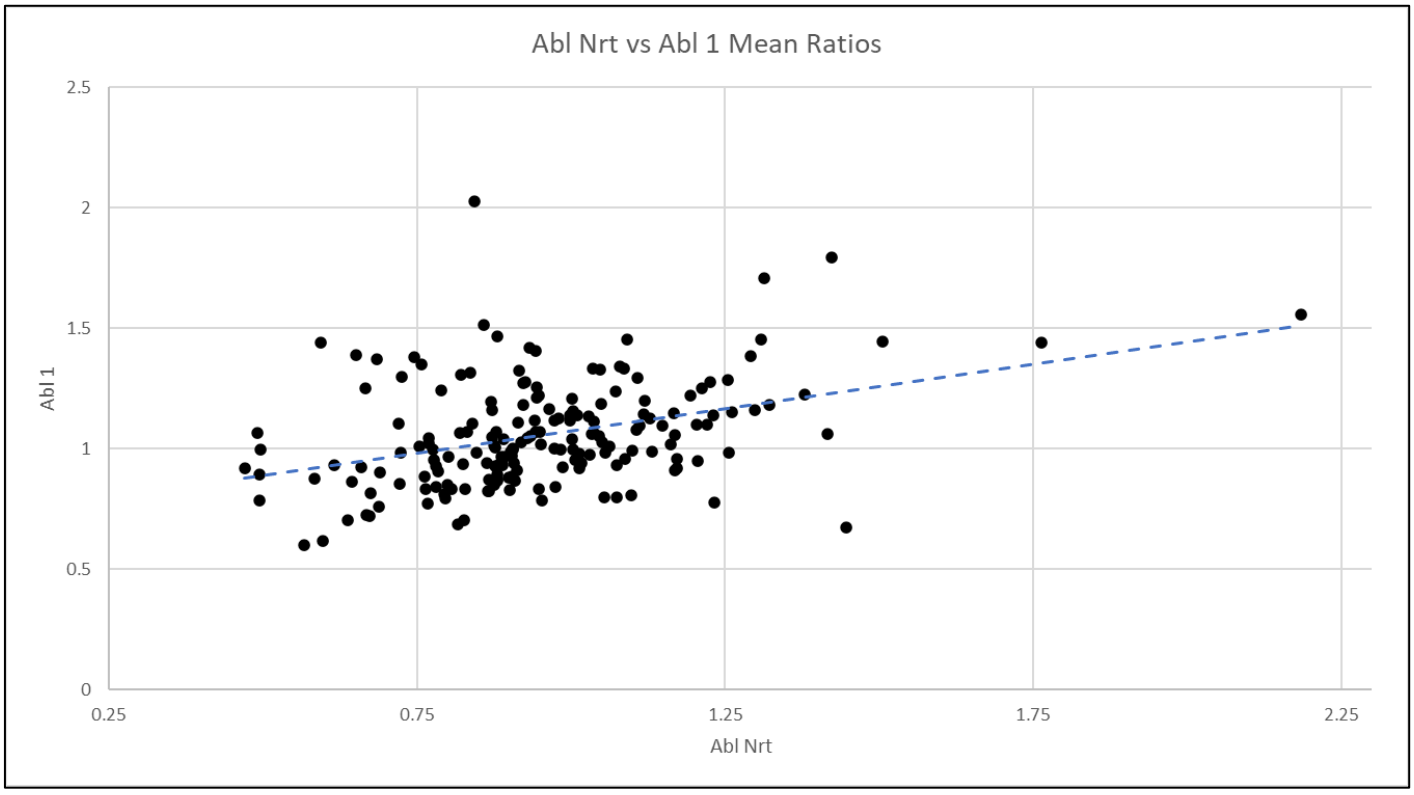

Figure 6. A graph of Abl Nrt's mean Tb+/Tb- ratio vs the mean Tb+/Tb- ratio of Delta 14.

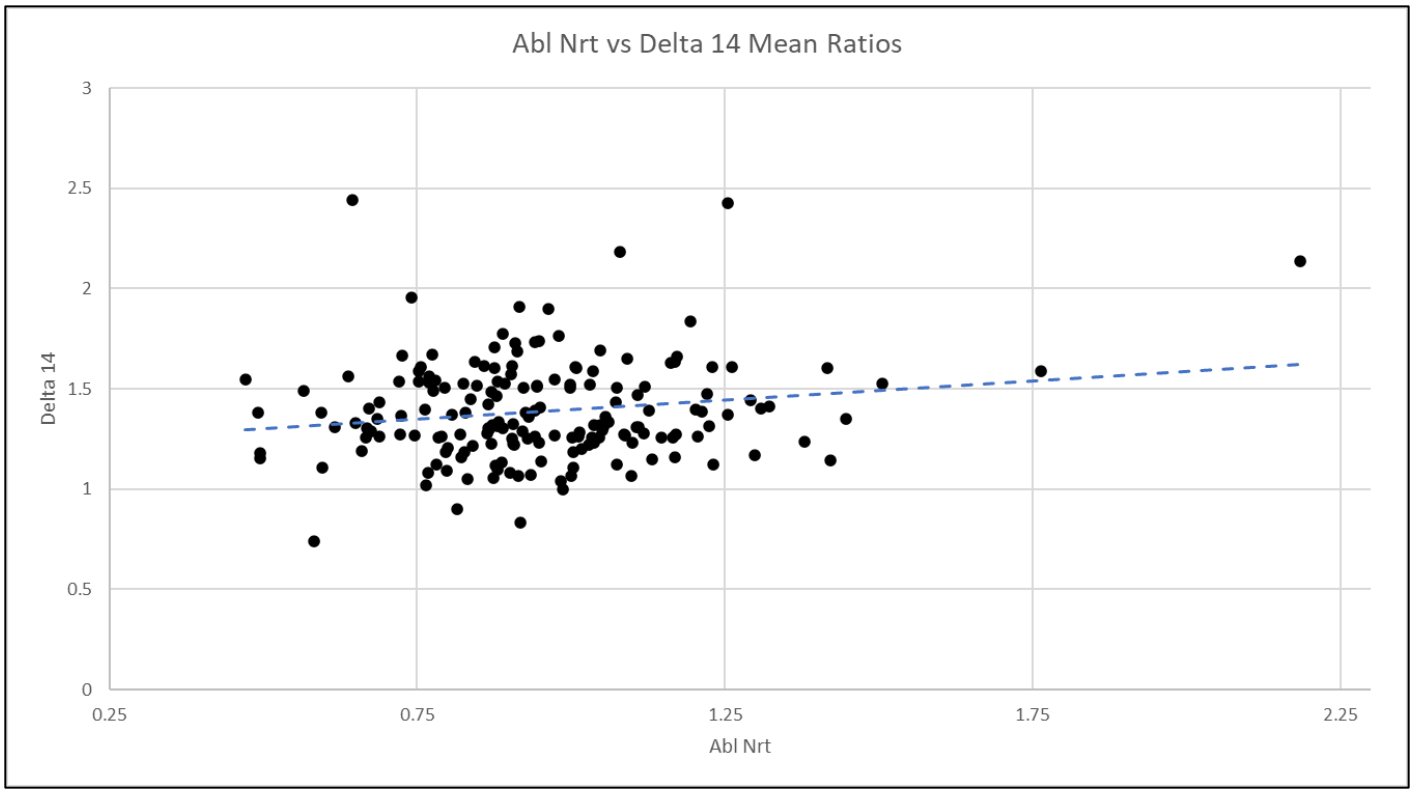

Figure 7. A graph of Abl Nrt's mean Tb+/Tb- ratio vs the mean Tb+/Tb- ratio of Rescue.

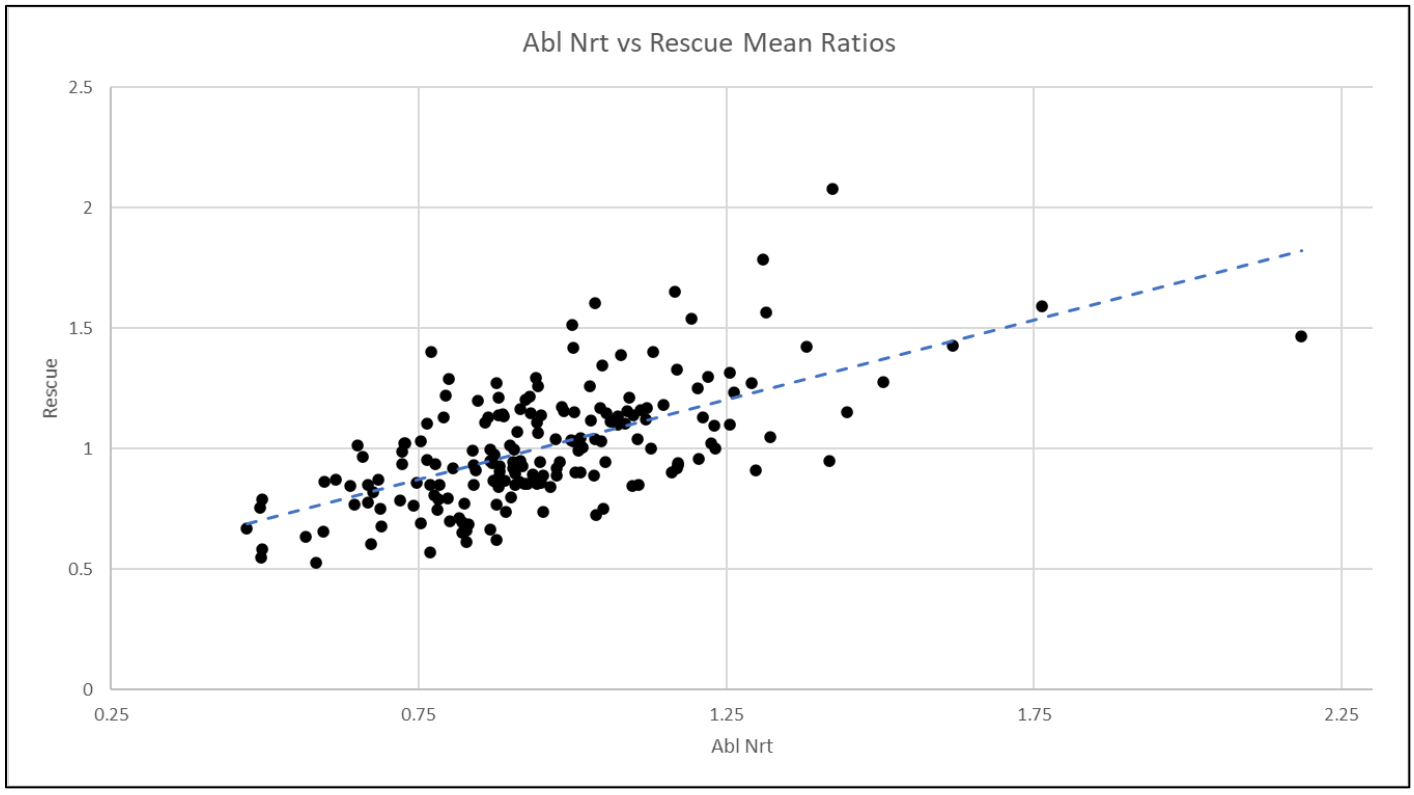

Figure 8. A graph of Abl 1's mean Tb+/Tb- ratio vs the mean Tb+/Tb- ratio of Abl 4.

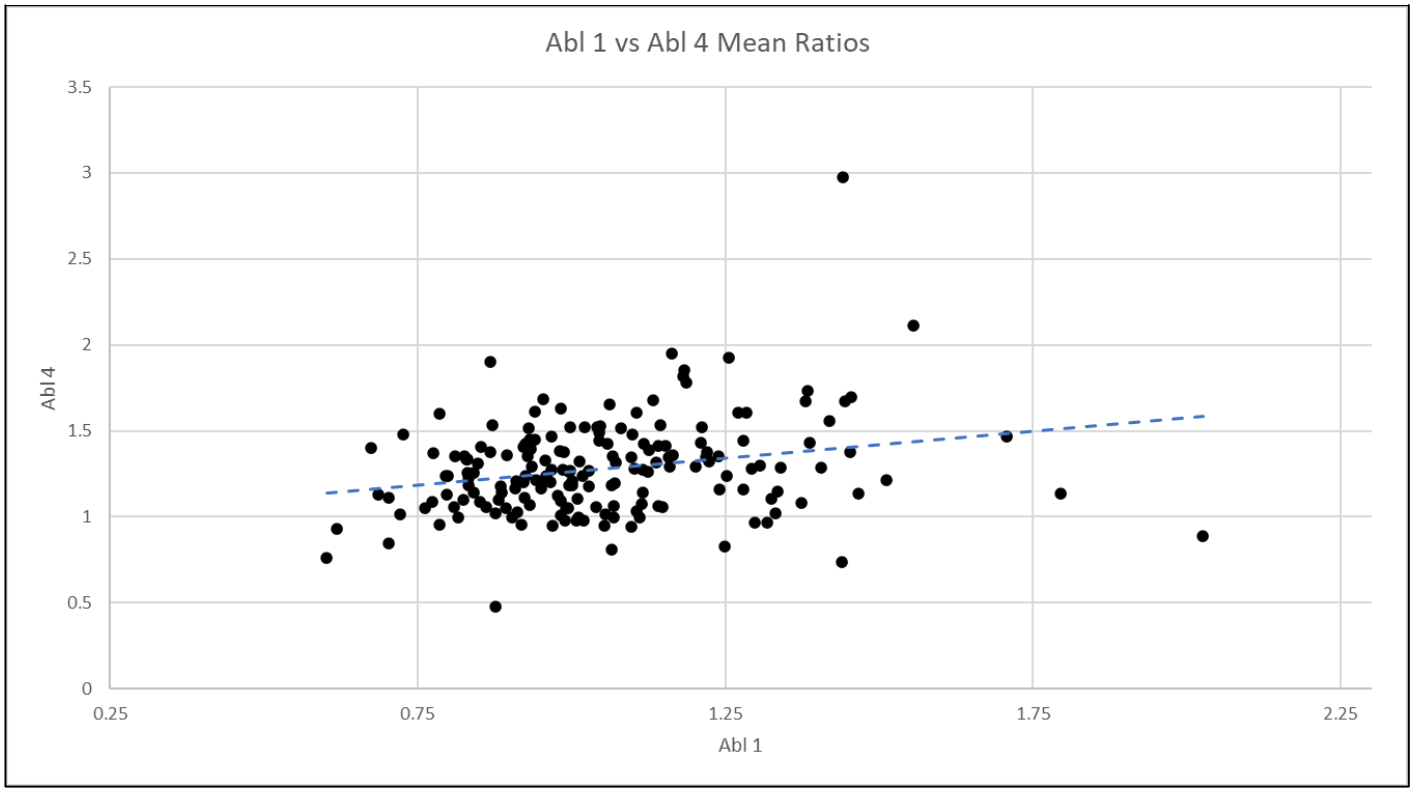

Figure 9. A graph of Abl 1's mean Tb+/Tb- ratio vs the mean Tb+/Tb- ratio of Rescue.

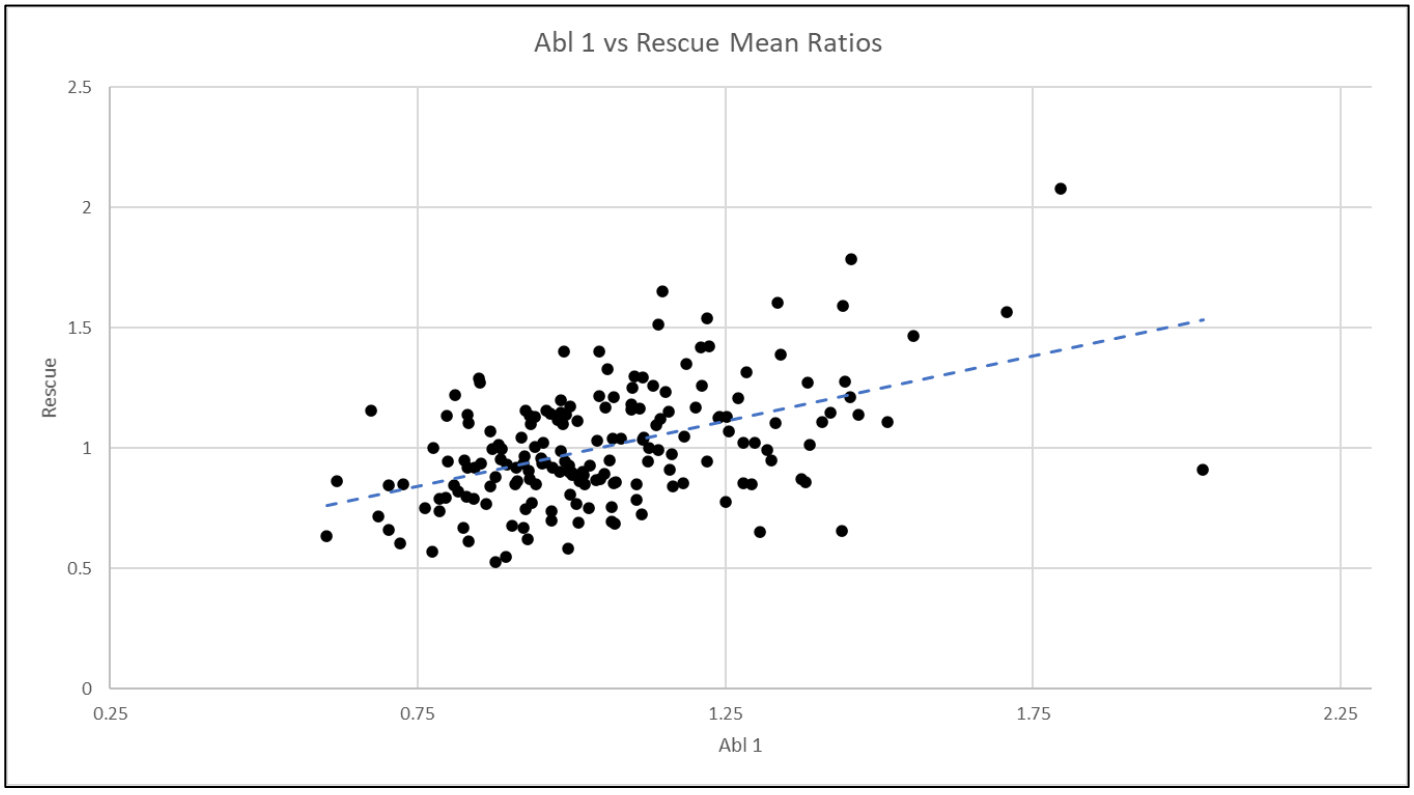

Figure 10. A graph of Abl 1's mean Tb+/Tb- ratio vs the mean Tb+/Tb- ratio of Delta14.

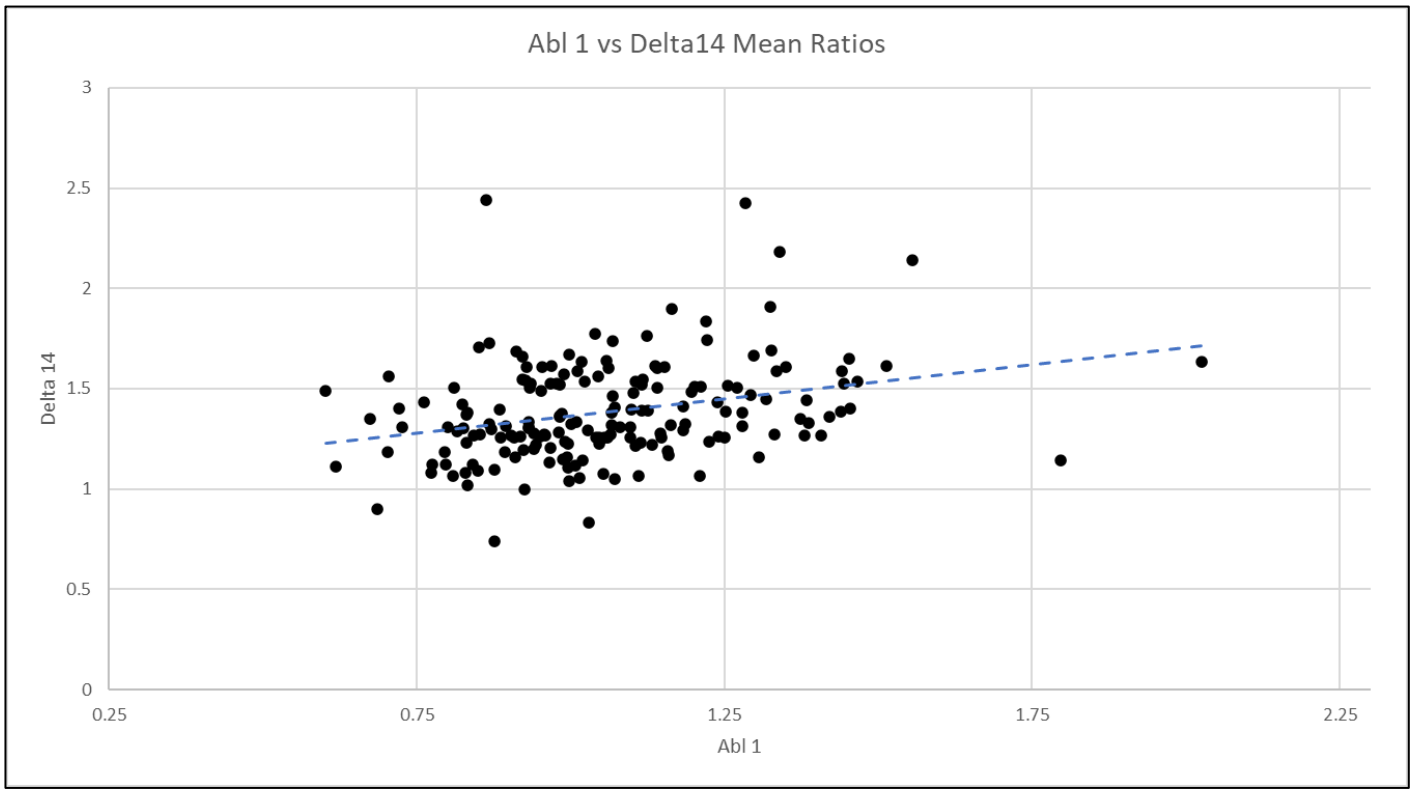

Figure 11. A graph of Abl 4's mean Tb+/Tb- ratio vs the mean Tb+/Tb- ratio of Delta14.

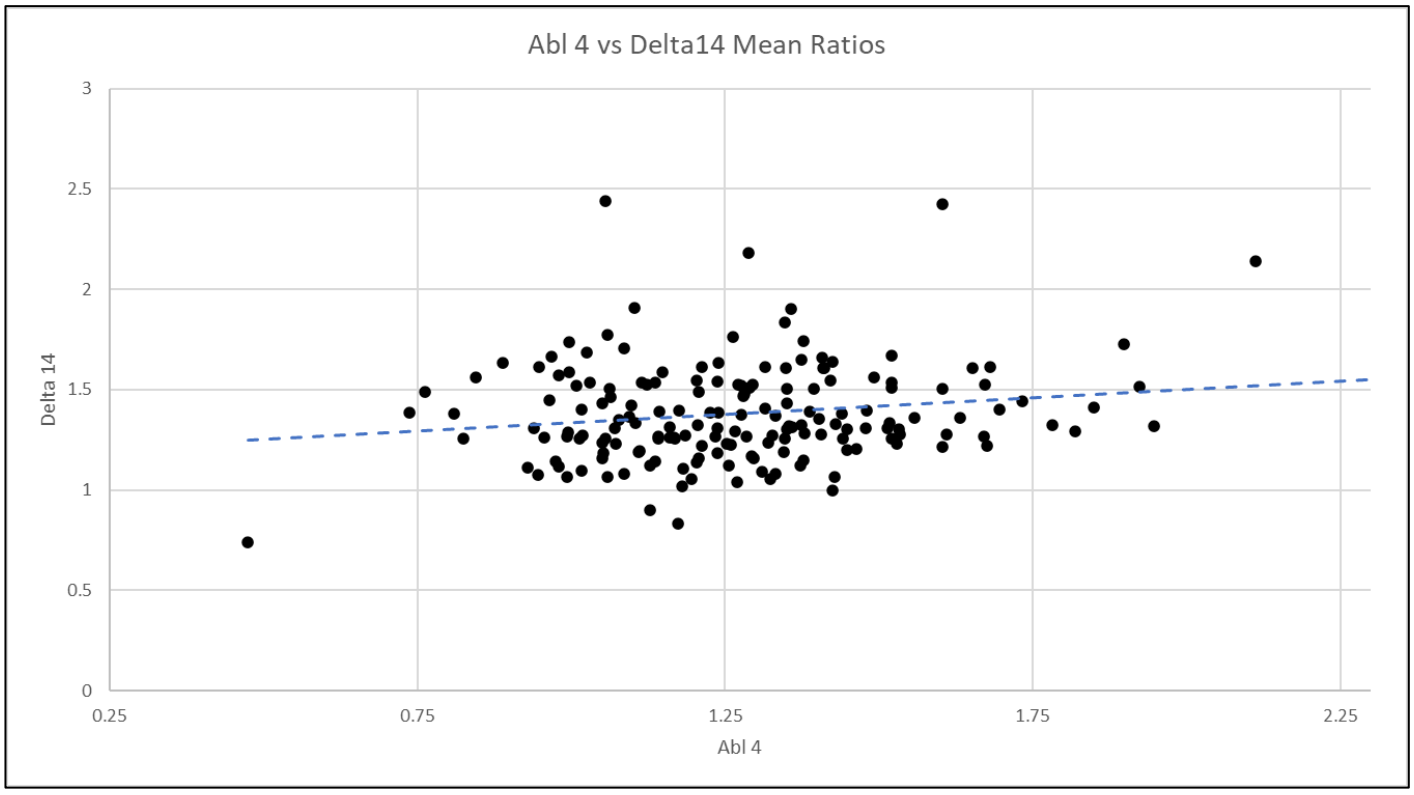

Figure 12. A graph of Abl 4's mean Tb+/Tb- ratio vs the mean Tb+/Tb- ratio of Rescue.

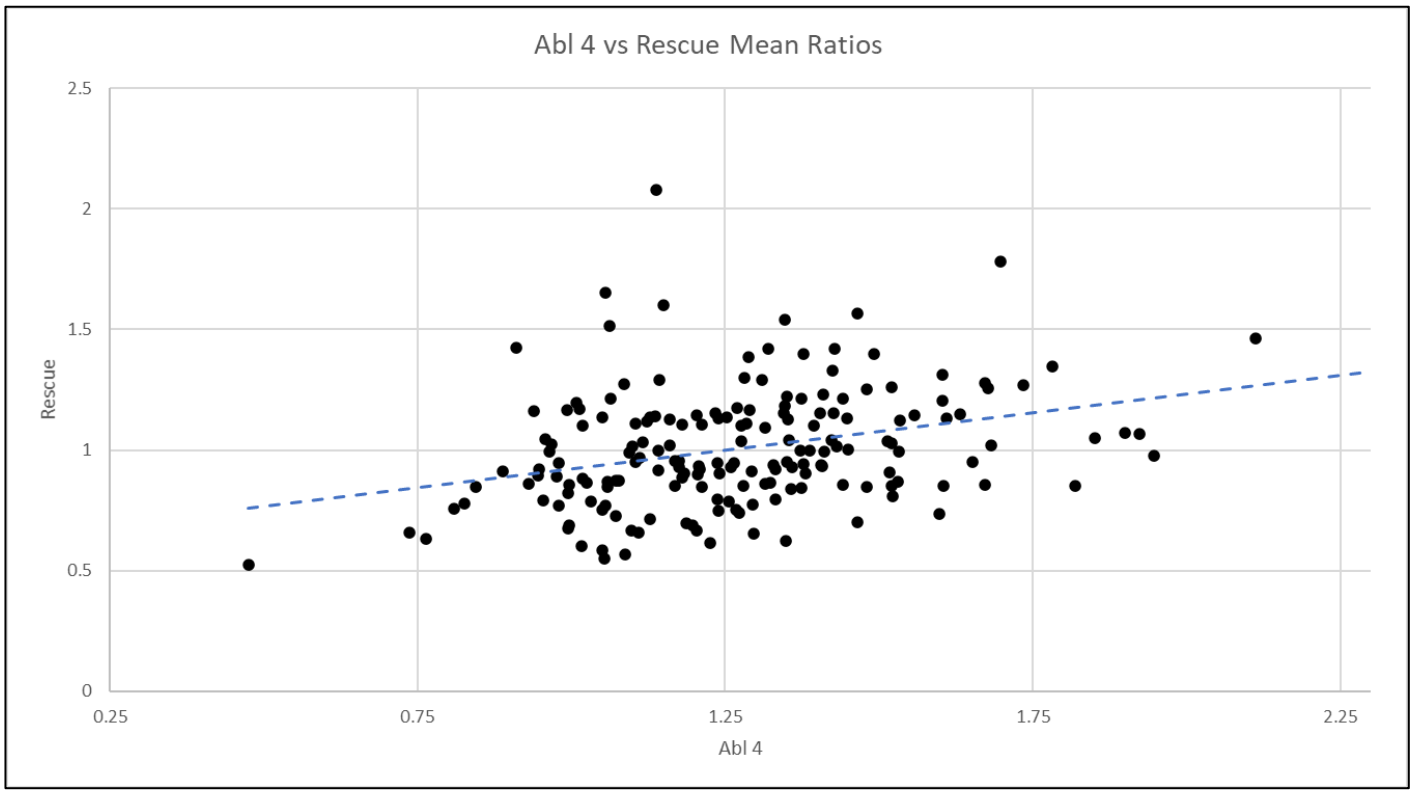

Figure 13. A graph of Rescue's mean Tb+/Tb- ratio vs the mean Tb+/Tb- ratio of Delta14.

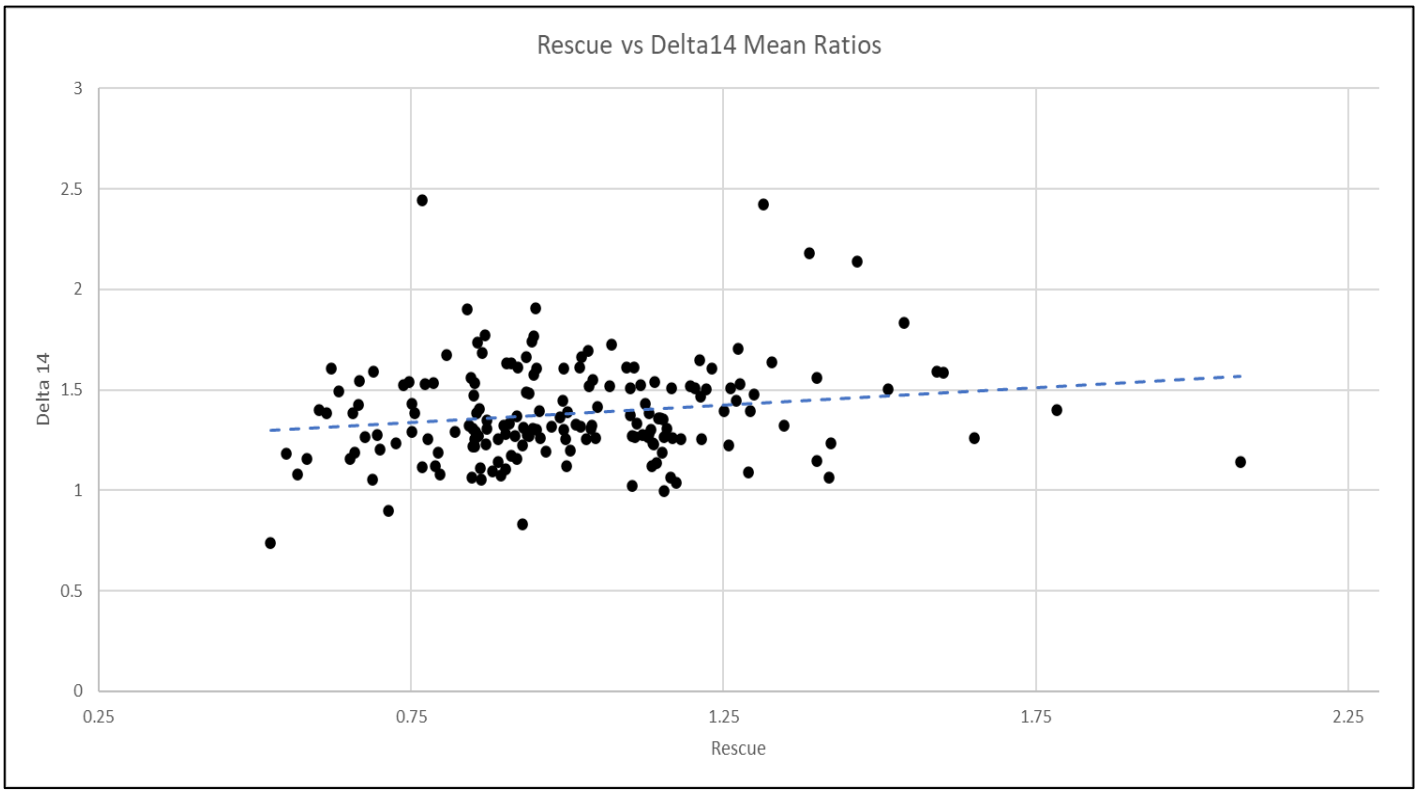

Figure 14. A graph of Abl Nrt's mean Tb+/Tb- ratio vs the mean Dr+/Dr- ratio of Abl Nrt.

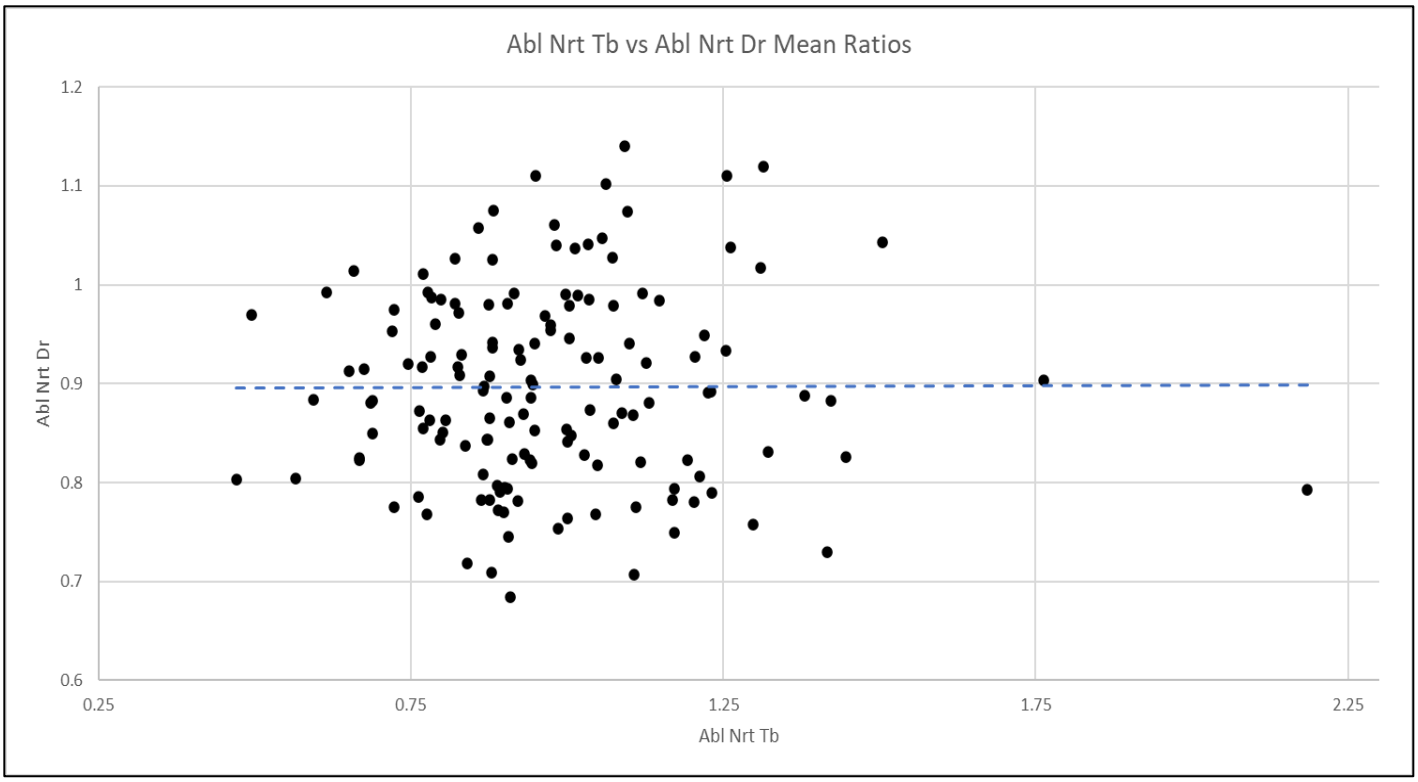

Table 7. SNP results from a GWA analysis of DGRP lines paired with their mean ratios.

Genotype	SNP	Site Annotation	Gene	p value
Abl 1	X_10193006_SNP	Intron	alpha-Man-I	1.15E-06
Abl 1	X_4521824_SNP	Intron	CG12184	8.99E-06
Abl 1	X_4521853_SNP	Intron	CG12184	4.25E-06
Abl 1	3R_14723142_SNP	Upstream	CG14297	3.00E-06
Abl 1	3R_14723267_SNP	Upstream	CG14297	1.91E-06
Abl 1	3R_14723258_SNP	Upstream	CG14297	7.05E-07
Abl 1	X_13201576_SNP	Downstream	CG15745	6.99E-06
Abl 1	3L_1903262_SNP	Intron	CG1887	9.19E-06
Abl 1	2L_2205183_SNP	Non Synonymous Coding	CG31668	5.00E-06
Abl 1	3L_7866076_SNP	Intron	CG32365	1.43E-05
Abl 1	2L_2195621_DEL	Intron	CG34172	5.79E-06
Abl 1	2L_3198519_DEL	Intron	CG34393	4.75E-06
Abl 1	3R_10944375_SNP	Intron	CG42788	7.95E-06
Abl 1	2R_13630036_SNP	Synonymous Coding	CG4996	4.29E-06
Abl 1	3R_12945910_SNP	Intron	cher	4.00E-06
Abl 1	X_8901408_SNP	Intron	CR43836	1.78E-05
Abl 1	3L_21677670_INS	Exon	CR43978	1.26E-06
Abl 1	2L_4078420_SNP	Intron	ed	5.03E-06
Abl 1	2R_13198804_SNP	Intron	mbl	9.82E-06
Abl 1	2R_13198828_SNP	Intron	mbl	9.82E-06
Abl 1	3L_2743665_SNP	Intron	Mrtf	7.98E-06
Abl 1	3L_2743681_SNP	Intron	Mrtf	1.08E-06
Abl 1	2L_14043429_DEL	Intron	nAcRalpha-34E	1.18E-05
Abl 1	3R_2987891_SNP	Upstream	sas	9.21E-06
Abl 1	3L_6506233_DEL	Intron	sfl	2.82E-05
Abl 1	2L_20632586_SNP	Intergenic Modifier		2.12E-05
Abl 1	2R_20226597_SNP	Intergenic Modifier		2.07E-05
Abl 1	3L_10793231_SNP	Intergenic Modifier		1.29E-05
Abl 1	2R_20226558_SNP	Intergenic Modifier		1.10E-05
Abl 1	2L_6850647_SNP	Intergenic Modifier		7.61E-06
Abl 1	2R_14082654_SNP	Intergenic Modifier		6.65E-06
Abl 1	3L_21680814_SNP	Intergenic Modifier		4.45E-06
Abl 1	2R_20226667_SNP	Intergenic Modifier		3.15E-06
Abl 1	2R_13825524_SNP	Intergenic Modifier		1.49E-06
Abl 4	3R_16378803_SNP	Intron	att-ORFB	1.90E-05
Abl 4	3L_1042346_INS	Intron	bab1	1.17E-06
Abl 4	X_20946743_SNP	Intron	bves	9.23E-06
Abl 4	X_19615267_SNP	Intron	CG12531	1.05E-05
Abl 4	3L_18593750_SNP	3' UTR	CG13380	1.29E-05
Abl 4	3L_18593641_SNP	3' UTR	CG13380	4.56E-06
Abl 4	3R_7561628_SNP	Intron	CG14721	9.58E-06
Abl 4	2R_3619580	Intron	CG18812	5.88E-06
Abl 4	X_4793872_SNP	Intron	CG42594	7.01E-06
Abl 4	X_745972_SNP	Intron	CG43867	3.57E-06

Table 7. (continued).

Genotype	SNP	Site Annotation	Gene	p value
Abl 4	2L_8154522_SNP	Intron	CG8552	1.26E-05
Abl 4	3R_10268936_SNP	Intron	cv-c	4.47E-06
Abl 4	3L_16436401_SNP	Intron	dsx-c73A	9.83E-06
Abl 4	3L_9261249_SNP	Intron	GluRIB	5.43E-06
Abl 4	3L_9260043_SNP	Intron	GluRIB	1.87E-06
Abl 4	X_16653061_DEL	Intron	if	8.38E-06
Abl 4	2L_14666405_SNP	Intron	osp	1.03E-05
Abl 4	2L_14666407_SNP	Intron	osp	7.65E-06
Abl 4	2L_14666459_SNP	Intron	osp	7.18E-06
Abl 4	2L_14666419_SNP	Intron	osp	3.44E-06
Abl 4	2L_14666453_SNP	Intron	osp	4.08E-07
Abl 4	3R_4939989_SNP	Intron	pum	1.23E-07
Abl 4	2L_6968058_SNP	Upstream	smt3	6.46E-06
Abl 4	2L_6968053_SNP	Upstream	smt3	5.90E-06
Abl 4	2R_15955051_SNP	Intergenic Modifier		9.34E-06
Abl 4	3L_6795225_INS	Intergenic Modifier		5.91E-06
Abl 4	3L_7194572_SNP	Intergenic Modifier		5.13E-06
Abl 4	2L_3443544_SNP	Intergenic Modifier		4.71E-06
Abl 4	2L_5515293_SNP	Intergenic Modifier		3.19E-06
Abl 4	3L_18579826_SNP	Intergenic Modifier		1.21E-06
Abl Nrt	3R_452144_SNP	Intron	5-HT2	2.50E-06
Abl Nrt	3R_13081440_INS	Intergenic Modifier	beat-IIb	3.87E-06
Abl Nrt	2L_15299282_SNP	3' UTR	CG15262	7.55E-06
Abl Nrt	X_18343963_SNP	Intron	CG32547	7.64E-06
Abl Nrt	X_13439407_SNP	Downstream	Cpr12A	9.26E-06
Abl Nrt	3L_4081058_DEL	Intron	Gad1	9.15E-06
Abl Nrt	X_19221619_DEL	Downstream	gfA	1.57E-05
Abl Nrt	2R_2404838_SNP	Intron	jing	7.56E-07
Abl Nrt	2R_6949002_SNP	Intron	luna	3.23E-07
Abl Nrt	2R_13131235_INS	Intron	mbl	5.23E-06
Abl Nrt	3R_5856468_SNP	Intron	Mical	1.98E-06
Abl Nrt	3L_18641137_SNP	Intron	MYPT-75D	1.05E-05
Abl Nrt	2L_11882638_SNP	Intron	Pde1c	9.20E-06
Abl Nrt	2L_11882650_SNP	Intron	Pde1c	3.16E-06
Abl Nrt	2L_11882664_SNP	Intron	Pde1c	1.90E-06
Abl Nrt	2R_4545473_SNP	Intron	ptc	1.31E-05
Abl Nrt	2R_3186402_SNP	Synonymous Coding	pwn	3.03E-06
Abl Nrt	3L_5895489_SNP	Synonymous Coding	QC	5.07E-06
Abl Nrt	3L_5895517_SNP	Non Synonymous Coding	QC	3.29E-06
Abl Nrt	3L_5895533_SNP	5' UTR	QC	2.45E-06
Abl Nrt	2R_19527421_SNP	Intron	retn	8.30E-06
Abl Nrt	2R_14824531_SNP	Intron	sano	7.82E-06
Abl Nrt	2R_14824549_SNP	Intron	sano	9.00E-08
Abl Nrt	2L_19814596_SNP	Intron	sick	5.71E-06

Table 7. (continued).

Genotype	SNP	Site Annotation	Gene	p value
Abl Nrt	2L_6232623_SNP	Intergenic Modifier		5.96E-06
Abl Nrt	2R_4520739_SNP	Intergenic Modifier		5.60E-06
Abl Nrt	2R_4520738_SNP	Intergenic Modifier		4.61E-06
Abl Nrt	2L_12576072_SNP	Intergenic Modifier		2.25E-06
Delta14	2R_5995863_SNP	Downstream	14-3-3zeta	2.05E-06
Delta14	X_3478978_SNP	Intron	AlstR	1.93E-05
Delta14	X_3478986_SNP	Intron	AlstR	6.82E-06
Delta14	2L_19769020_SNP	Upstream	bsh	6.59E-07
Delta14	2L_5808191_SNP	Synonymous Coding	CG11034	1.11E-05
Delta14	2L_5808173_SNP	Synonymous Coding	CG11034	8.62E-06
Delta14	3R_9679352_SNP	Downstream	CG14362	3.57E-05
Delta14	X_6125243_SNP	Synonymous Coding	CG14446	5.26E-06
Delta14	X_21064284_SNP	5' UTR	CG14579	2.71E-05
Delta14	X_21064242_SNP	Upstream	CG14579	2.01E-05
Delta14	X_10225342_SNP	Synonymous Coding	CG15306	7.81E-06
Delta14	3L_7863864_SNP	Intron	CG32365	9.80E-06
Delta14	2L_6128168_SNP	3' UTR	CG42730	2.82E-05
Delta14	2R_6252189_SNP	Intron	CG42732	2.19E-05
Delta14	2L_18242977_DEL	Intron	CG42750	3.62E-06
Delta14	3R_4415464_SNP	Intron	CG42796	5.98E-06
Delta14	3L_16491090_SNP	Intron	CG43373	7.20E-06
Delta14	X_10061190_DEL	Intron	CG43902	4.24E-06
Delta14	X_10061189_SNP	Intron	CG43902	1.79E-06
Delta14	2R_6671828_SNP	Intron	CG44299	2.96E-06
Delta14	2R_13680251_SNP	Upstream	CG5036	3.55E-09
Delta14	2L_5773913_INS	Intron	CG9171	8.52E-07
Delta14	2R_18160451_SNP	Intron	dve	2.69E-06
Delta14	2L_5556123_SNP	Synonymous Coding	GluRIIA	9.13E-06
Delta14	2L_1013523_SNP	3' UTR	IA-2	3.94E-05
Delta14	2R_6397049_SNP	Downstream	lola	8.34E-06
Delta14	2R_6397130_SNP	Downstream	lola	8.34E-06
Delta14	2R_9962168_SNP	Intron	Prosap	8.84E-06
Delta14	2R_6448839_SNP	Intron	psq	2.76E-07
Delta14	2L_7520090_	Intron	Rapgap1	1.20E-05
Delta14	3L_4917435_SNP	Intron	Rh50	3.94E-06
Delta14	3L_8549157_SNP	Intron	rhea	2.24E-07
Delta14	3L_15908998_SNP	Intron	sff	9.87E-06
Delta14	3L_7259421_SNP	3' UTR	unc-13-4A	4.25E-06
Delta14	2L_989924_SNP	Intergenic Modifier		3.01E-05
Delta14	3L_6261365_SNP	Intergenic Modifier		2.61E-05
Delta14	2R_10602584_SNP	Intergenic Modifier		2.01E-05
Delta14	2R_6442595_SNP	Intergenic Modifier		1.64E-05
Delta14	3L_6636135_SNP	Intergenic Modifier		1.36E-05
Delta14	2R_16265426_SNP	Intergenic Modifier		8.97E-06

Table 7. (continued).

Genotype	SNP	Site Annotation	Gene	p value
Delta14	3L_6263512_SNP	Intergenic Modifier		8.95E-06
Delta14	X_22220738_SNP	Intergenic Modifier		6.19E-06
Delta14	3L_9235814_DEL	Intergenic Modifier		6.14E-06
Delta14	X_22220947_SNP	Intergenic Modifier		5.84E-06
Delta14	X_5405646_SNP	Intergenic Modifier		5.74E-06
Delta14	2L_19288915_SNP	Intergenic Modifier		4.27E-06
Delta14	3L_6266317_SNP	Intergenic Modifier		3.52E-06
Delta14	2L_19290707_SNP	Intergenic Modifier		3.25E-06
Delta14	2L_19290709_SNP	Intergenic Modifier		9.86E-07
Delta14	2R_17666060_SNP	Intergenic Modifier		6.28E-07
Rescue	2L_13935475_SNP	Intron	Ance-3	8.30E-06
Rescue	2L_13935478_SNP	Intron	Ance-3	5.41E-06
Rescue	2L_13935547_SNP	Intron	Ance-3	4.29E-06
Rescue	2L_13935530_SNP	Intron	Ance-3	3.63E-06
Rescue	2L_12177013_DEL	Intron	atilla	6.17E-08
Rescue	3R_6152798_SNP	Non Synonymous Coding	Bruce	3.13E-06
Rescue	2R_10733938_SNP	Synonymous Coding	CG10209	1.58E-06
Rescue	2L_12759949_SNP	Downstream	CG15483	1.19E-06
Rescue	3L_1903264_DEL	Intron	CG1887	2.59E-06
Rescue	3L_13056820_SNP	Intron	CG34429	1.24E-05
Rescue	3L_17627550_SNP	Intron	CG7497	3.05E-06
Rescue	3R_10219158_SNP	Non Synonymous Coding	cv-c	7.43E-06
Rescue	X_3705492_SNP	Upstream	ec	8.66E-06
Rescue	3L_14341635_SNP	Intron	fz	4.98E-06
Rescue	3R_6367531_SNP	Intron	hth	4.83E-06
Rescue	3L_5374763_SNP	Intron	Ir64a	4.80E-06
Rescue	3L_5374692_INS	Intron	Ir64a	2.64E-07
Rescue	2L_18130113_SNP	3' UTR	kel	8.32E-06
Rescue	2L_6152446_SNP	Synonymous Coding	Muc26B	2.45E-06
Rescue	2L_6152028_SNP	5' UTR	Muc26B	1.09E-08
Rescue	2L_6152034_SNP	5' UTR	Muc26B	1.08E-08
Rescue	3R_12998339_SNP	Intron	Mur89F	5.47E-06
Rescue	2L_11882664_SNP	Intron	Pde1c	1.35E-06
Rescue	2L_11882650_SNP	Intron	Pde1c	6.99E-07
Rescue	2R_10207978_SNP	Intron	Shroom	2.94E-06
Rescue	3L_5691605_SNP	Intron	sif	8.54E-06
Rescue	X_5256297_SNP	Intron	SK	1.04E-05
Rescue	X_5256299_SNP	Intron	SK	1.04E-05
Rescue	3L_11679041_SNP	Intron	Sug	5.82E-06
Rescue	3L_11679933_SNP	Synonymous Coding	Sug	4.05E-06
Rescue	3L_11679811_SNP	Intron	Sug	4.77E-08
Rescue	2L_3104089_SNP	Intron	toc	9.83E-06
Rescue	2L_6003150_SNP	3' UTR	Tsp26A	2.38E-06
Rescue	3R_9708318_SNP	Intergenic Modifier		1.01E-05

Table 7. (continued).

Genotype	SNP	Site Annotation	Gene	p value
Rescue	3L_15662022_SNP	Intergenic Modifier		9.52E-06
Rescue	3R_10785767_SNP	Intergenic Modifier		8.95E-06
Rescue	3L_15660911_SNP	Intergenic Modifier		8.10E-06
Rescue	2L_12767079_SNP	Intergenic Modifier		7.47E-06
Rescue	3L_15660667_SNP	Intergenic Modifier		6.66E-06
Rescue	2R_12735629_SNP	Intergenic Modifier		4.91E-06
Rescue	2L_14532447_SNP	Intergenic Modifier		3.58E-06
Rescue	2L_12762869_SNP	Intergenic Modifier		3.05E-06
Rescue	2L_12766472_SNP	Intergenic Modifier		6.42E-07
Rescue	2L_12765670_SNP	Intergenic Modifier		2.21E-07
Rescue	2L_12764490_SNP	Intergenic Modifier		1.30E-07

Table 8. Genes where SNPs occurred that were shared between genotypes.

Genotype	SNP	Site Annotation	Gene	p value
Abl 1	3L_1903262_SNP	Intron	CG1887	9.19E-06
Rescue	3L_1903264_DEL	Intron	CG1887	2.59E-06
Abl 1	3L_7866076_SNP	Intron	CG32365	1.43E-05
Delta14	3L_7863864_SNP	Intron	CG32365	9.80E-06
Abl 4	3R_10268936_SNP	Intron	cv-c	4.47E-06
Rescue	3R_10219158_SNP	Non Synonymous Coding	cv-c	7.43E-06
Abl 1	2R_13198804_SNP	Intron	mbl	9.82E-06
Abl 1	2R_13198828_SNP	Intron	mbl	9.82E-06
Abl Nrt	2R_13131235_INS	Intron	mbl	5.23E-06
Abl Nrt	2L_11882664_SNP	Intron	Pde1c	1.90E-06
Abl Nrt	2L_11882650_SNP	Intron	Pde1c	3.16E-06
Abl Nrt	2L_11882638_SNP	Intron	Pde1c	9.20E-06
Rescue	2L_11882650_SNP	Intron	Pde1c	6.99E-07
Rescue	2L_11882664_SNP	Intron	Pde1c	1.35E-06

Acknowledgements

I would like to thank all members of my thesis committee, especially my mentor Dr. Mark Seeger. His constant feedback and assistance were directly responsible for the completion of this thesis, and his enthusiasm for research is responsible for my decision to start a career in science. I would also like to thank Meredith Zhang, who was responsible for much of the pupae scoring that occurred before the Covid-19 pandemic. I thank my other lab mates who have since graduated but assisted in the beginnings of this project.

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